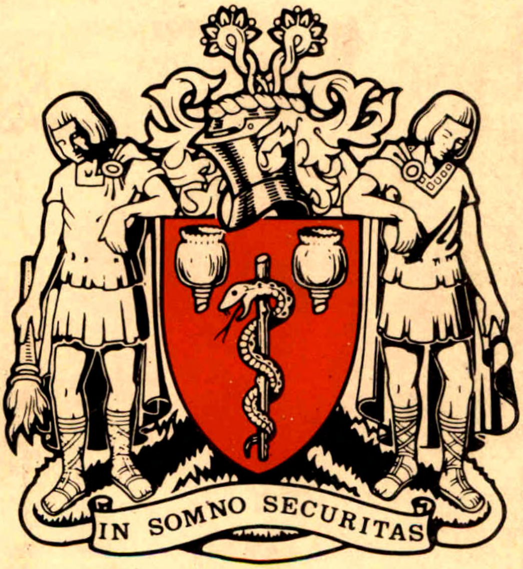
Acc.
25.9.87

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain & Ireland

Volume 41 Number 1 January 1986

(1)



LIBRARY

Published for
The Association of Anaesthetists of Great Britain and Ireland by
Academic Press Grune & Stratton
London Orlando San Diego New York Toronto
Montreal Sydney Tokyo

ISSN 0003-2409

'Everyday hundreds of people put their trust in our equipment. We can't afford to ever let them down'

Today, health care organisations around the world rely on the quality range of Ohmeda medical equipment and know their trust is well founded.

For over 60 years we have committed ourselves to developing the world's finest medical equipment and to building up an established network of specialists dedicated to research and development, manufacture, quality control and after sales service.

This means that everytime you choose Ohmeda, we're standing right by you to offer advice on new products, to service existing equipment and most importantly to provide you with the help and assistance you need to perform at your best, all of the time.

Specify Ohmeda — we won't let you down.

SPECIALIST CARE FOR SPECIALIST PEOPLE.

Ohmeda

Ohmeda
Elizabeth Way Harlow Essex CM19 5AB England
0279 29692 Telex 81497

BOC Health Care

P, 24, 519

CUK-H03420-9-P024519

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

Editorial Board
Editor J. N. LUNN
Assistant Editors M. MORGAN, C. E. BLOGG, R. GREENBAUM, R. M. JONES
Chairman P. J. HELLIWELL
Advisory Editors R. S. ATKINSON, T. B. BOULTON
Members JEAN LUMLEY, C. F. SCURR, P. J. F. BASKETT and a representative of the Junior Anaesthetists Group
Ex officio
The President of the Association T. B. BOULTON
The Honorary Treasurer of the Association M. M. BURROWS
The Honorary Secretary of the Association M.T. INMAN
The Immediate Past Honorary Secretary of the Association W. R. MACRAE

Editor Emeritus C. LANGTON HEWER

Sub-editors of special sections
L. KAUFMAN Anaesthetic literature
A. PADFIELD National and local events
G. D. PARBROOK Audiovisual reviews
M. J. HARRISON Computer programs
JACQUELINE WELCH, DIANE WINTERBURN Reference librarians
D. V. BATEMAN Honorary proof reader

Address for literary contributions Dr J. N. Lunn, The Editor, *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK [telephone Cardiff (0222) 755944 Ext. 3101].

Neither the Editor nor the Association of Anaesthetists of Great Britain and Ireland is in any way responsible for the statements made or the views expressed by contributors.

Investigations performed on man must conform to appropriate ethical standards including voluntary consent and acceptance by an ethical committee.

Published monthly (January–December) at 24–28 Oval Road, London NW1 7DX, England by Academic Press Inc. (London) Limited for the Association of Anaesthetists of Great Britain and Ireland, Rooms 475–478, Tavistock House South, Tavistock Square, London WC1H 9LG. As from December 2nd 1985, 9 Bedford Square, London WC1B 3RA.

1985, Volume 40, 12 issues. Inland, £72.50 inclusive of postage and packing; abroad, $189.00 inclusive of postage and packing. Subscription orders should be sent to Academic Press Inc. (London) Limited, High Street, Foots Cray, Sidcup, Kent DA14 5HP (Tel. 01-300-0155), with the exception of those originating in the U.S.A., Canada, Central America and South America; these should be sent to Grune & Stratton Inc., 111 Fifth Avenue, New York, NY 10003, U.S.A. Send notices of change of address to the office of the Publishers at least 6–8 weeks in advance. Please include both old and new addresses.

U.S.A. Postmaster: send address changes to Anaesthesia, Grune & Stratton Inc., 111 Fifth Avenue, New York, NY 10003, U.S.A.

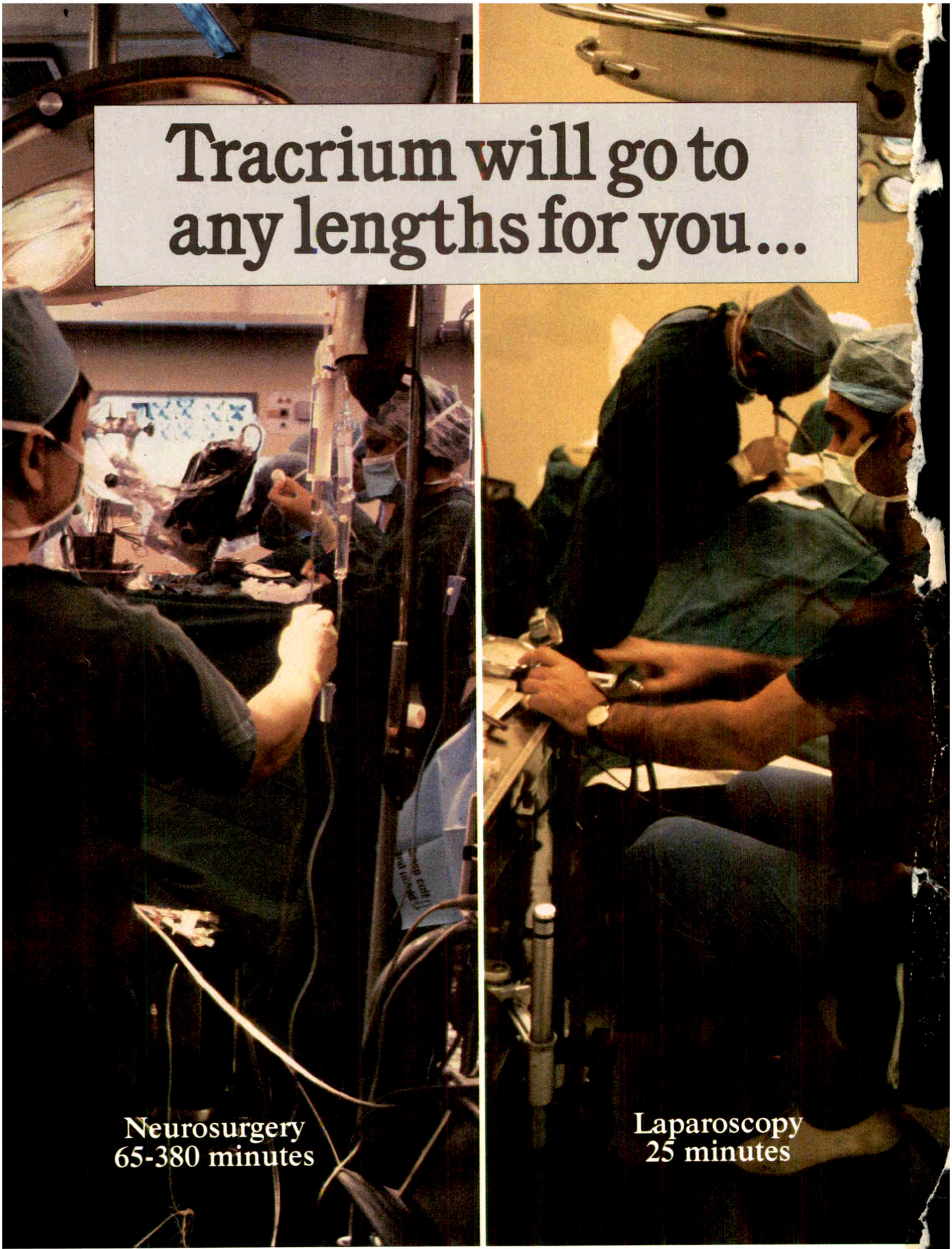
Application to pay at second class postage rates pending at Jamaica, New York 11431, U.S.A.

Air freight and mailing in the U.S.A. by Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, U.S.A.

© 1985 The Association of Anaesthetists of Great Britain and Ireland. The appearance of the code at the bottom of the first page of a paper in this journal indicates the copyright owner's consent that copies of the paper may be made for personal or internal use, or for the personal or internal use of specific clients in the U.S.A. This consent is given on the condition, within the U.S.A., that the copier pay the stated per-copy fee through the Copyright Clearance Center Inc., 27 Congress Street, Salem, MA 01970, U.S.A. for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, for resale or for copying or distributing copies outside the U.S.A.

ISSN 0003-2409

LIBRARY



ALMIC MEDICAL
DIVISION
HE WELLCOME FOUNDATION LTD

With Tracrium there are no cumulative effects with supplemental dosing, so the pattern of block and recovery remains consistent, regardless of the number of doses given.

Surgical muscle relaxation can therefore be conveniently extended at a uniform level for as long as required, simply by repeated incremental bolus doses given at predictable clock-timed intervals or by continuous i.v. infusion.

The rate of recovery remains just as rapid as that seen after administration of a single bolus dose, so reversal can be promptly and easily achieved whatever the duration of the operation – regardless of the patient's age and hepatic, renal and circulatory status.

All of which adds up to an unusual degree of versatility.

That's why more and more anaesthetists are using Tracrium routinely, in procedures of widely differing type and length, from laparoscopy to open-heart surgery.

Wellcome

Muscle relaxation without cumulation.

TRACRIUM

Atracurium besylate

(Prescribing information overleaf.)

*Trade Mark

Tracrium Prescribing Information

Uses Tracrium is a highly selective, competitive (non-depolarising) muscle relaxant for use in a wide range of surgical procedures and to facilitate control of respiration. Tracrium is highly suitable for endotracheal intubation, especially where subsequent relaxation is required.

Dosage and administration

Intravenous injection: Adults and children over 1 year: 0.3-0.6 mg/kg depending on the duration of block required; this will provide relaxation for about 15-35 minutes. Tracrium may be used at standard dosage in elderly patients and in those with respiratory, hepatic or renal failure. Full block can be prolonged with supplementary doses of 0.1-0.2 mg/kg as required. Successive supplementary dosing does not give rise to cumulation. Endotracheal intubation can usually be accomplished within 90 seconds of intravenous injection of 0.5-0.6 mg/kg. The neuromuscular block produced by Tracrium can be rapidly and permanently reversed by standard doses of neostigmine which should be preceded by the administration of atropine. Recovery from full block without the use of neostigmine occurs in about 35 minutes.

Continuous infusion: Tracrium is suitable for administration by continuous infusion at rates of 0.005-0.01 mg/kg/minute (0.3-0.6 mg/kg/hour) to maintain neuromuscular block during long surgical procedures. Tracrium maintains acceptable physical and chemical stability in daylight at concentrations of between 0.5 and 0.9 mg/ml at 30°C for up to: 4 hours in: Compound Sodium Lactate Intravenous Infusion B.P.; 8 hours in: Ringer's Injection U.S.P.; Glucose Intravenous Infusion B.P. 5% w/v; Sodium Chloride 0.18% w/v and Glucose Intravenous Infusion B.P. 4% w/v and up to 24 hours in: Sodium Chloride Intravenous Infusion B.P. Tracrium can be administered by infusion during cardiopulmonary bypass surgery, at the recommended infusion rate. Induced hypothermia to a body temperature of 25 to 26°C reduces the rate of inactivation of atracurium, therefore full neuromuscular block may be maintained by approximately half the original infusion rate at these temperatures.

Contra-indications, warnings, etc. Contra-indicated in patients hypersensitive to atracurium besylate. Tracrium should be used with caution in patients receiving aminoglycosides or polypeptide antibiotics and in patients with myasthenia gravis. In common with all other neuromuscular blocking agents, adequate facilities must be available for endotracheal intubation and artificial ventilation. The neuromuscular block produced by Tracrium may be increased by the concomitant use of inhalational anaesthetics such as halothane. Tracrium should not be mixed in the same syringe with any other agent; in particular it must not be mixed with thiopentone or any alkaline agent, as the high pH would cause inactivation of the Tracrium. As with all other neuromuscular blocking agents the possibility of transient hypotension due to histamine release cannot be excluded. Although animal studies have indicated that Tracrium has no adverse effects on foetal development, nevertheless, like all neuromuscular blocking agents, it should be used with caution in pregnant women. Tracrium may be used to maintain neuromuscular relaxation in Caesarean section as atracurium does not cross the placenta in clinically significant amounts.

Presentation Tracrium injection contains 10 mg per ml atracurium besylate. Two ampoule sizes, 2.5 ml and 5 ml, are available.

Basic NHS costs £6.50 for a box of 5 x 2.5 ml ampoules. £12.50 for a box of 5 x 5 ml ampoules. (PL3/0166).

Further information is available on request.

Calmic Medical Division
The Wellcome Foundation Ltd
Crewe, Cheshire

Wellcome

TRACRIUM

Atracurium besylate

CALMIC MEDICAL
DIVISION

ACADEMIC PRESS

AP AP

publishes books and journals in many areas of Science including:

Acoustics, Agriculture,
Anatomy, Anthropology,
Archaeology, Audiology

Biochemistry, Biology, Botany

Cancer research, Cardiology,
Chemistry, Computer science

Economics, Engineering,
Environmental science

Food Science

Geography, Geology

Immunology

Materials technology,
Mathematics, Microbiology

Neuroscience, Nutrition

Oncology, Ornithology

Pathology, Pharmacology,
Physics, Physiology,
Psychiatry, Psychology

Religion

Sociology, Speech, Surgery

Toxicology

Virology

Zoology

BOOKS AND JOURNALS

24-28 Oval Road, London NW1 7DX, U.K.
Orlando, FL 32887, USA.

'EUROPA'
ANAESTHETIC EQUIPMENT

ILLUSTRATED IS THE NEW MK II EUROPA WITH OPTIONAL MID-SHELF MONITORING FACILITY.

Built to high standards of design and finish, the Tricomed EUROPA is able to provide the most comprehensive specification demanded in modern anaesthesia.

TRIcoMED®

Tricomed Limited, 5-7 Sydenham Road, London, SE26 5ET, England.
Telephone 01-778 1165 Telex 8955141 TRIMED

Tricomed Pty Limited, 21 Shepherd Street, Marrickville, NSW 2204,
Australia. Telephone 2 569 1585

Tricomed (Hong Kong) Limited, 4th floor, Anson House, 61 Wyndham Street,
GPO Box 7625, Hong Kong. Telephone 5 248003

WEST MIDLANDS
INTENSIVE CARE GROUP

6th ANNUAL MEETING ON

INTENSIVE CARE

8th–9th April, 1986, at Wyddrington Hall, University of Birmingham

This course is designed for members of all specialities and all grades having an interest in Intensive Care.

The first day will be largely concerned with the management of aspects of respiratory care.

The morning of the second day will be concerned with infections treated and acquired on the Intensive Care Unit and the afternoon with fluid and renal problems.

Guest speaker – DR. M. BRANTHWAITE

Course fee £65 or £35 per day including coffee, tea, lunch and the course dinner on the 8th April, but exclusive of accommodation.

Full details from: Miss Megan Wood, Postgraduate Secretary, Postgraduate Centre, East Birmingham Hospital, Bordesley Green East, Birmingham B9 5ST.

LEICESTER DEPARTMENT OF ANAESTHESIA
F.F.A.R.C.S. EXAMINATION (PART 3)

Revision Course

A whole time course of lectures and tutorials

21 APRIL–25 APRIL 1986

FEE £35 *(except doctors employed in the Trent Region)*

Further Information:

The Secretary: Department of Anaesthesia, The Leicester Royal Infirmary,
Leicester, LE1 5WW. Tel: 0533 541414 Ext. 474

Other courses in Anaesthesia for the F.F.A.R.C.S. Examination:

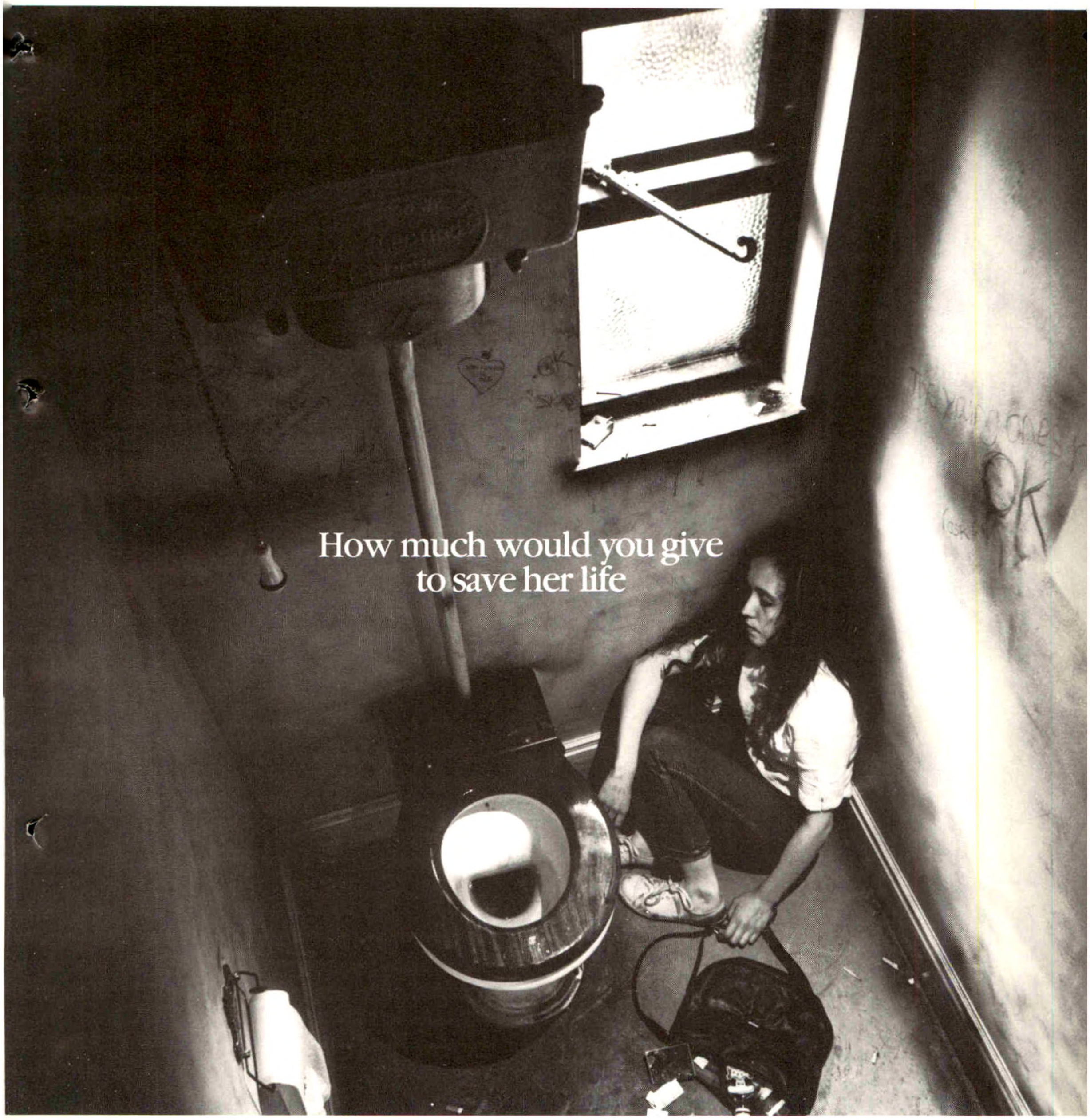
Part 1 Whole time lecture course, 3 February–7 February 1986

Part 2 Half-day Friday afternoons, 11 October–11 April 1986

Part 3 Clinical measurement Friday afternoons, 5 September–17 October 1986
Revision practicals Friday afternoons, 2 May–27 June 1986

Further information from the Department of Anaesthesia, The Leicester Royal Infirmary

Prescribing Information: Presentation: Narcan* (1ml ampoules and 10ml vials) – each 1ml of solution contains 0.4mg naloxone hydrochloride. Narcan* Neonatal (2ml ampoules) – each 1ml of solu
contains 0.02mg naloxone hydrochloride. **Uses:** Diagnosis and reversal of respiratory and other CNS effects of opioids, including those in the newborn following opioid administration to the moth
Dosage and Administration: Adults: For opioid overdose give 0.4mg to 2mg intravenously. Repeat at 2 to 3 minute intervals if required. For post-operative use give 0.1-0.2mg intravenously allowin
minutes between each 0.25ml (0.1mg) increment. In certain circumstances (eg. overdosage of long-acting opioid) give intravenous infusion. Dilute in 0.9% saline or 5% dextrose in water or saline (2mg
Narcan in 500ml = 0.004mg/ml). Use infusion mixtures within 24 hours. Titrate infusion according to response. **Children:** For opioid overdose, initially 0.01mg (10 micrograms) per kg intravenou
repeating with 0.1mg (100 micrograms) per kg if response unsatisfactory. **Neonates:** Establish adequate airway first. Usually 0.01mg/kg i.v., i.m. or s.c. for opioid-induced depression, repeated as for ad
guidelines. Alternatively give a single intramuscular dose of 200 micrograms at birth. **Contra-Indications:** Hypersensitivity to Narcan. **Precautions, Warnings:** A withdrawal syndrome may occur in opio
dependent patients, neonates delivered of such patients, and chronic opioid users. Usual precautions in pregnancy. Keep patients under observation as Narcan has a short duration of action and rep
doses may be necessary. Care in patients with compromised cardiac function as there are two reports of ventricular tachycardia and fibrillation. **Adverse Effects:** Occasionally, nausea and vomiti
especially when larger than recommended doses used. **Product Licence Nos.:** Narcan – Ampoule. 4524/0001. Narcan – Vial. 4524/0001. Narcan Neonatal. 4524/0002. **NHS Price:** Narcan – Ampoule (b
of 10 x 1ml amps). £46.21. Narcan – Vial (1 x 10ml vial). £41.59. Narcan Neonatal (box of 10 x 2ml amps). £33.54. Further information is available on request from the company. Du Pont (UK) Limit
Pharmaceuticals, Wedgwood Way, Stevenage, Hertfordshire SG1 4QN. Telephone: (0438) 734549. *Narcan is a registered trademark of E.I. Du Pont de Nemours & Co. Inc.


How much would you give
to save her life

For a known or suspected opioid overdose, the initial adult dose of Narcan* is 0.4-2.0mg i.v. repeated, if necessary, up to 10mg.

These larger doses of Narcan may be necessary to diagnose the presence of opioids such as dextropropoxyphene, whose respiratory depressant effects in overdose are particularly hard to reverse.

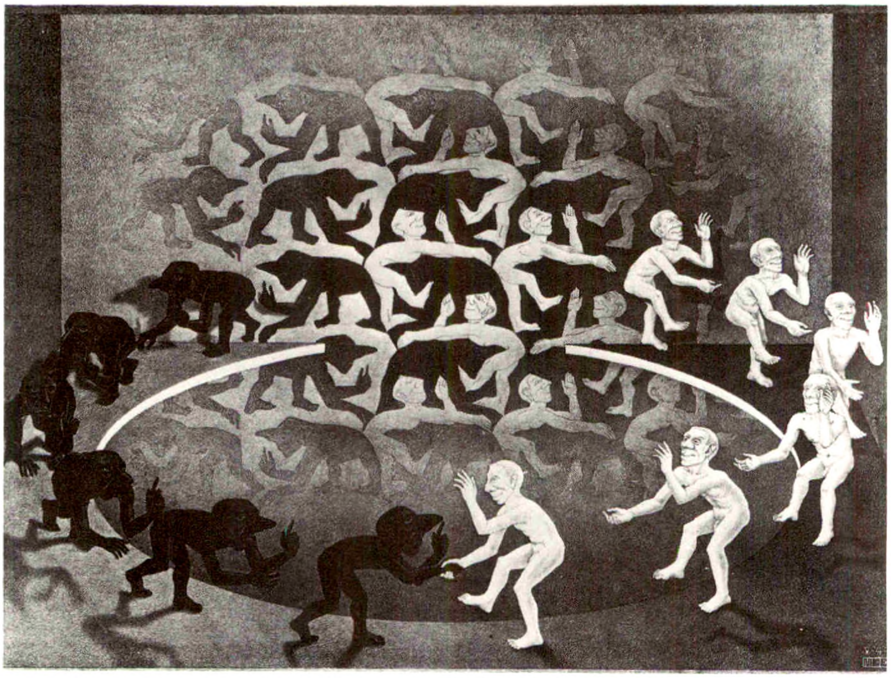
Overdoses caused by long-acting opioids, such as methadone, may necessitate repeated administration of Narcan to prevent recurrent narcosis.

In both these situations, the new Narcan 10ml vial offers a convenient alternative to existing 1ml ampoules. The 10ml vial also greatly simplifies the administration of Narcan by infusion.

NARCAN*
(naloxone hydrochloride)

New 10ml vial
Same strength,
larger volume

Du Pont Pharmaceuticals



© M C Escher Heirs c/o Cordon Art - Baarn - Holland

Complete the Circle

. . . in Anaesthetic Agent Monitoring with

THE NORMAC –
ANAESTHETIC AGENT MONITOR

Dual beam infrared absorption technique. Patented water separation system. 0.6 second response time. Alarm. Analogue display/recorder output.

- **Accurate**
- **Unaffected by humidity**
- **Easy calibration**
- **Adaptable**

For an early demonstration contact:
Nick Tyrrell, Product manager, Vickers Medical,
Priestley Road, Basingstoke, Hants. RG24 9NP.
Telephone: 0256 29141

Vickers Medical

Anaesthesia, 1986, Volume 41, pages 1–3

Editorial

Transdermal hyoscine (scopolamine) and postoperative vomiting

There has been no real reduction, during the last 50 years, in the incidence of nausea and vomiting following anaesthesia and surgery, despite continuing improvements in anaesthetic techniques. In his retrospective study of 10 000 patients in 1936, Waters quoted an incidence of postoperative nausea and vomiting of 40.6%,[1] and similar results have been reported in recent prospective studies.[2,3] These unwanted effects are often distressing and they occur in patients who, in many cases, will have undergone only minor surgical procedures. In a recent review, Palazzo and Strunin[4,5] concluded that postoperative nausea and vomiting are rarely the result of a single factor, and that for this reason their prevention and treatment may be far from easy.

There are five main groups of anti-emetic drugs currently available: antihistamines (promethazine, cyclizine), phenothiazines (perphenazine, prochlorperazine) butyrophenones (droperidol, haloperidol), other dopamine antagonists (metoclopramide, domperidone), and the anticholinergic drugs (hyoscine and atropine). Of these, the anticholinergics are probably still the most widely used; for example, Mirakhur *et al.* found that they were favoured by some 69% of anaesthetists in the United Kingdom.[6] The use of atropine as an anti-emetic was first described in 1883 by Brown-Séquard (reported in Burtles and Peckett[7]), but there have been few controlled studies of the efficacy of atropine or hyoscine in the treatment of postoperative vomiting. Riding showed that intramuscular atropine (0.6 mg), given before the anaesthetic, reduced postoperative nausea and vomiting by 50% when used alone, and by 47% when given with morphine (10 mg).[8] Subsequent studies of atropine (0.6 mg) and hyoscine (0.4 mg) administered in combination with opiates have confirmed their short-lived anti-emetic actions.[9,10] Hyoscine is the more effective of the two, but its effects are outlasted by the emetic properties of morphine.

The disadvantages of hyoscine when given by the intramuscular route are twofold. Firstly, the relative rapidity of its absorption leads to a high incidence of dose-related adverse effects. Secondly, its short half life (about one hour) results in a rapid dissipation of its action. Attention has therefore turned to the development of a slow-release formulation of hyoscine, which could, when applied to the skin, deliver the drug to the body at a slow, steady rate, thus reducing the incidence of its adverse effects and prolonging the duration of its therapeutic effects.

It has been known for many years that the skin does not pose a barrier to the absorption of certain drugs. The occurrence of the systemic adverse effects of corticosteroids when applied to the skin under occlusive dressings is recognised as evidence.[11] The ease with which a drug penetrates the skin depends on the integrity of the skin, the area to which the drug is applied, interindividual and regional differences in the quality of the skin, and certain physicochemical characteristics of the drug itself, for example, lipophilicity, low molecular weight, pH in solution.[12] It has been shown that, for hyoscine, absorption is best via the postauricular skin, and the application of hyoscine to that area in a preformulated slow-release patch is supposed to result in delivery of drug to the body at a rate which depends on the formulation and not on the nature of the skin itself.[13] Pharmacokinetic studies have shown that the urinary excretion of hyoscine following the application of a single patch is similar to that seen during continuous low-dose intravenous infusion, and that the drug continues to be absorbed for up to 3 days after initial application.[12] One would therefore expect that hyoscine, when administered in this fashion, would provide prolonged protection, as it does in motion sickness, against postoperative nausea and vomiting, with a low incidence of adverse effects. That it does not provide prolonged protection is suggested by the results of the double-blind placebo-controlled study reported by Uppington and his colleagues in the present issue (p. 16).

The use of transdermal hyoscine for the prevention of postoperative nausea and vomiting in this way

0003–2409/86/010001 + 03 $0.03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

is not new. In a double-blind, placebo controlled comparison with intramuscular hyoscine, Jackson *et al.* showed that pre-operative sedation was greater after intramuscular administration, but there was no improvement in postoperative nausea and vomiting.[14] A placebo controlled study in children showed no difference in the incidence of postoperative vomiting, but there was an unacceptably high incidence (5 out of 24 children) of pre-operative adverse effects, namely extreme agitation and hallucinations.[15] In contrast to these two studies, the present study has shown that transdermal hyoscine reduced the incidence of nausea and vomiting compared with placebo, although there was no significant reduction in the treated group in the number of doses of metoclopramide required in the postoperative period. Furthermore, the duration of the therapeutic effect was short, only 24 hours, and the overall incidence of severe nausea and vomiting in the treated patients over the whole 72-hour study period was as high as in the untreated patients (68.4%).

The reasons for these disappointing results are not clear, particularly the failure of transdermal hyoscine to protect against nausea and vomiting for more than 24 hours. However, there are possible pharmacokinetic and pharmacodynamic explanations, assuming that the patches used were pharmaceutically reliable. Firstly, it has been shown that although release of hyoscine from transdermal patches is uniform, as judged by urinary hyoscine excretion from 24–84 hours after initial application, there is a peak of higher urinary excretion at 12–24 hours after application. The lack of therapeutic effect after 24 hours may therefore simply have been due to the failure of the system to provide high enough plasma concentrations during that time after the initial peak. Secondly, it is possible that some unidentified factors interfered with the pharmacological effects of the drug after 24 hours, although the careful matching of the treated patients with controls should have minimised effects of that kind. Thirdly, it is possible that the patients developed tolerance to the effects of hyoscine after 24 hours, as has been suggested in patients being treated for motion sickness.[16]

Whatever the reasons for the poor therapeutic outcome, the next step should be a study of the efficacy of transdermal hyoscine given at intervals of 24 hours, since there was certainly evidence in the current study that unwanted effects were few. In this way, it may prove possible to improve the mode of administration and thus to achieve increased therapeutic benefit from this formulation, particularly if the initially faster rate of release is important. Furthermore, such a study would also test the hypothesis of the occurrence of pharmacological tolerance after 24 hours of continuous administration, and could thus provide information of great pharmacological interest. Ideally, studies of this kind should also include plasma or at least urinary hyoscine concentration measurements as part of their design in further elucidation of these questions, and this is an undoubted defect of the studies reported here.

Until more evidence of this kind becomes available, the use of hyoscine, either intramuscularly or by transdermal patch, should not be regarded as a first line approach in the prevention of postoperative nausea and vomiting.

MRC Unit and University Department of Clinical Pharmacology J.K. ARONSON

Nuffield Department of Anaesthetics, J.W. SEAR
Radcliffe Infirmary,
Oxford OX2 6HE

References

1. WATERS RM. The present status of cyclopropane. *British Medical Journal* 1936; **2:** 1013–7.
2. KORTTILA K, KAUSTE A, AUVINEN J. Comparison of domperidone, droperidol and metoclopramide in the prevention and treatment of nausea and vomiting after balanced general anesthesia. *Anesthesia and Analgesia* 1979; **58:** 396–400.
3. MORTENSEN PT. Droperidol (Dihydrobenzperidol) post-operative anti-emetic effect when given intravenously to gynaecological patients. *Acta Anaesthesiologica Scandinavica* 1982; **26:** 48–52.
4. PALAZZO MGA, STRUNIN L. Anaesthesia and emesis. I: etiology. *Canadian Anaesthetists' Society Journal* 1984; **31:** 178–87.
5. PALAZZO MGA, STRUNIN L. Anaesthesia and emesis. II: prevention and management. *Canadian Anaesthetists' Society Journal* 1984; **31:** 407–15.

6. Mirakhur RK, Clarke RSJ, Dundee JW, McDonald JR. Anticholinergic drugs in anaesthesia. A survey of the present position. *Anaesthesia* 1978; **33:** 133–8.
7. Burtles R, Peckett BW. Post-operative vomiting. *British Journal of Anaesthesia* 1957; **29:** 114–23.
8. Riding JE. Post-operative vomiting. *Proceedings of the Royal Society of Medicine* 1960; **53:** 671–7.
9. Dundee JW, Moore J, Clarke RSJ. Studies of drugs given before anaesthesia. V: Pethidine 100 mg alone or with atropine or hyoscine. *British Journal of Anaesthesia* 1964; **36:** 703–10.
10. Clarke RSJ, Dundee JW, Love WJ. Studies of drugs given before anaesthesia. VIII: Morphine 10 mg alone or with atropine or hyoscine. *British Journal of Anaesthesia* 1965; **37:** 772–7.
11. Miller JA, Munro DD. Topical corticosteroids: clinical pharmacology and therapeutic use. *Drugs* 1980; **19:** 119–34.
12. Shaw JE. Transdermal drug delivery: potentials and limitations. In: Lemberger L, Reidenberg MM, eds. *Proceedings of the second world conference on clinical pharmacology and therapeutics*. 1983. Bethseda, Maryland: American Society for Pharmacology and Experimental Therapeutics, 1984: 444–58.
13. Shaw J, Urquhart J. Programmed systemic drug delivery by the transdermal route. *Trends in Pharmacological Sciences* 1980; **1:** 208–11.
14. Jackson SH, Schmitt L, McGuire J, Hall M. Transdermal scopolamine as a preanaesthetic drug, and postoperative antinauseant and antiemetic. *Anesthesiology* 1982; **57:** A330.
15. Gibbons PA, Nicolson SC, Betts EK, Rosenberry KR, Jobes DR. Scopolamine does not prevent post-operative emesis after pediatric eye surgery. *Anesthesiology* 1984; **61:** A435.
16. Graybiel A, Cramer DB, Wood CD. Antimotion-sickness efficacy of scopolamine 12 and 72 hours after transdermal administration. *Aviation, Space and Environmental Medicine* 1982; **53:** 770–2.

Editorial notices

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

News and Notices sections

The first issue of each quarter will contain full News and Notices sections.

Copy dates for these will be: 14 March 1986 for June 1986, 13 June 1986 for September 1986 and 12 March 1986 for July 1986.

Supplementary News and Notices sections will be published in other issues but they will contain only material which requires publication before the next full News and Notices section.

Anaesthesia, 1986, Volume 41, pages 4–10

Thiopentone levels during cardiopulmonary bypass

Changes in plasma protein binding during continuous infusion

D. J. MORGAN, D. P. CRANKSHAW, P. R. PRIDEAUX, H. N. J. CHAN AND
M. D. BOYD

Summary

Plasma total and unbound concentrations of thiopentone were investigated during exponentially decreasing infusions in seven patients undergoing cardiopulmonary bypass. Total plasma thiopentone concentrations reached a plateau (10.2, SD 2.1 μg/ml) soon after the initial bolus dose and commencement of the infusion. Concentrations were maintained until the onset of cardiopulmonary bypass, whereupon total plasma thiopentone concentration fell abruptly to 50.0 (SD 5.8) percent of the prebypass level. The unbound fraction of thiopentone increased from 16.6 (SD 1.9) percent before bypass to a maximum of 29.3 (SD 5.6) percent during bypass ($p < 0.01$), decreased to 22.9 (SD 3.3) percent at the end of bypass ($p < 0.01$), but was still elevated 5–7 hours later (20.5, SD 2.5 percent). The result of the changes in binding was a smaller decline in unbound thiopentone concentration at the onset of bypass to 76.4 (SD 15.7) percent of the prebypass level. Also, unbound levels returned to the prebypass level by the end of bypass, whereas total levels remained low.

Key words

Anaesthetics, intravenous; thiopentone.
Surgery; cardiopulmonary bypass.

We have recently developed a method of administering thiopentone by exponential infusion, with which relatively constant plasma thiopentone concentrations are achieved. Extracorporeal circulation is associated with profound physiological changes, such as haemodilution, hypotension, hypothermia and diminished renal and hepatic function.[1] Such changes may influence drug disposition, resulting in either higher[2-4] or lower[5-12] plasma drug concentrations, depending on the particular drug. The aim of this study was to investigate the effect of cardiopulmonary bypass on total and unbound plasma thiopentone concentrations in patients undergoing cardiac surgery and receiving thiopentone as the primary hypnotic agent.

Methods

After obtaining institutional approval, seven consenting adult male patients of mean age 57 years (range 35–73 years) and mean weight 79 kg

---

D.J. Morgan, MSc, PhD, Senior Lecturer in Pharmaceutics, H.N.J. Chan, M. Pharm, Postgraduate Student, Victorian College of Pharmacy, 381 Royal Parade, Parkville, D.P. Crankshaw, FFARACS, PhD, Senior Lecturer in Anaesthetics, M.D. Boyd, M.Appl.Sci. (Biophysics), Postgraduate Student, University Department of Surgery, The Royal Melbourne Hospital, Parkville, P.R. Prideaux, FFARACS, Staff Anaesthetist, Department of Anaesthetics, The Royal Melbourne Hospital, Parkville Victoria, Australia.

Correspondence should be addressed to Dr D.P. Crankshaw, University Department of Surgery, P.O. The Royal Melbourne Hospital, Victoria, Australia 3050.

0003–2409/86/010004 + 07 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

(range 74–88 kg) undergoing coronary artery bypass surgery were studied. None of the patients showed any clinical or biochemical evidence of hepatic or renal dysfunction. All patients were premedicated approximately 90 minutes before surgery, with either papaveretum 20 mg and hyoscine 0.4 mg or diazepam 5 mg and droperidol 5 mg. Prior to induction, some patients received up to 5 mg of diazepam intravenously to produce further sedation. Anaesthesia was induced by an intravenous bolus dose of thiopentone (1.49–1.92 mg/kg lean body mass) with the aim of achieving an initial plasma concentration close to the desired level. Each patient's lungs were mechanically ventilated after tracheal intubation. Anaesthesia was maintained with a mixture of nitrous oxide in oxygen (50–70 percent), intravenous fentanyl, pancuronium and thiopentone sodium. The infusion regimen for thiopentone was designed to achieve a constant plasma thiopentone concentration of about 15 μg/ml shortly after the bolus dose, and to maintain this concentration throughout surgery.

A constant plasma thiopentone concentration was achieved by infusing thiopentone at an exponentially decreasing rate, according to the general method described by Kruger-Thiemer.[13] In using this method, a linear mamillary three-compartment open model was assumed for the pharmacokinetics of thiopentone. The function I(t) describing the infusion was:

$$I(t) = (C_{ss}.\mathrm{Cl.LBM}/k_{10})(k_{10} + k_{12}\exp(-k_{21}t) + k_{13}\exp(-k_{31}t)) \qquad (1)$$

where C_{ss} is the desired steady-state plasma thiopentone concentration, Cl is the plasma clearance of thiopentone normalised to lean body mass (LBM) and k_{10}, k_{12}, k_{21}, k_{13} and k_{31} are parameters of the three-compartment model.[14] Population average parameter values for input to the equation were calculated by standard methods[14] from literature data,[15-18] and are shown in Table 1. The plasma clearance of thiopentone was normalised to lean body mass (LBM) in Table 1 by assuming that the mean LBM of all subjects in the cited studies[15-18] was 55 kg. The LBM of each of our patients was estimated by using the equation of Wulfsohn and Joshi:[19]

$$\%\ \text{fat} = 90 - 2\ (\text{height (inches)}—\text{girth (inches)}) \qquad (2)$$

$$\mathrm{LBM} = \frac{\mathrm{TBW}\ (100 - \%\ \text{fat})}{100} \qquad (3)$$

Table 1. Population mean pharmacokinetic parameters of thiopentone*

P′	8.29×10^{-5}/ml
A′	1.89×10^{-5}/ml
B′	6.80×10^{-6}/ml
π	0.231/minute
α	0.0141/minute
β	0.00127/minute
k_{12}	0.159/minute
k_{21}	0.0608/minute
k_{13}	0.0327/minute
k_{31}	0.00446/minute
k_{10}	0.0216/minute
Vd_{ss}	100 litres
Cl	2.87 ml/minute/kgLBM
Dose	347 mg
LBM†	55 kg

*P′, A′, B′ are dose corrected coefficients and π, α, β are hybrid rate constants of the tri-exponential equation describing thiopentone plasma concentrations following intravenous bolus administration. k_{12}, k_{21}, k_{13}, k_{31}, k_{10} are the rate constants for the classical three compartment model.[14]

†Assuming a mean population LBM of 55 kg.

Thiopentone was administered as a 2.5 percent solution of the sodium salt in water (for injections BP) via a syringe pump controlled by a Texas Instruments 980A minicomputer. Further details of the derivation of equation (1) and of the infusion method are presented by Crankshaw *et al.*[20]

Cardiopulmonary bypass was by extracorporeal roller pump (Polystan, Denmark) equipped with a disposable oxygenator (Bentley Bos 10 or Cobe–Optiflow II) and a heat exchanger. The priming solution consisted of 1 litre of an electrolyte solution (Plasmalyte 148 in 5% dextrose, Travenol Laboratories Pty Ltd), 1 litre of a fraction of pooled human plasma containing 50 g/litre total protein (Stable Plasma Protein Solution, Commonwealth Serum Laboratories, Melbourne), 60 mmol sodium bicarbonate, 2.5 mmol calcium chloride and 5000 units of heparin. Additional heparin was given before insertion of the caval and aortic cannulae. During cardiopulmonary bypass, pump flow rate was approximately 2.22 litres/minute/sq m; haematocrit fell to 0.22–0.30 and blood temperature was reduced to below 28°C. Rewarming was started approximately 30 minutes after commencement of bypass. After the termination of bypass, the effects of the heparin were reversed with protamine sulphate as monitored by the activated clotting time. Blood in the extracorporeal circuit was transfused back into the patient by slow intravenous infusion in the postbypass and recovery periods.

During the thiopentone infusion, 3-ml blood samples were collected into 10-ml lithium heparin tubes via the arterial cannula placed for blood pressure recording and blood gas determination. Samples were taken at 2–5 minute intervals during the first 10–15 minutes of bypass and, thereafter, approximately every 10 minutes until the end of the infusion. Blood samples were stored on ice and centrifuged at 1600 g for 5 minutes as soon as possible after collection, usually within 15 minutes. Plasma was analysed immediately for plasma protein binding determinations or stored frozen (− 5 to − 10° C) until analysis for total thiopentone. Unbound plasma thiopentone concentration was measured in selected samples throughout the study period. During cardiopulmonary bypass, unbound concentration was measured in alternate samples. In the remaining samples, unbound concentration was calculated using the average of the unbound fraction measured in neighbouring samples. Plasma thiopentone concentration was assayed by high pressure liquid chromatography.[17] The coefficient of variation for this assay was 3.2 percent ($n = 4$), 2.5 percent ($n = 4$) and 1.6 percent ($n = 4$) at plasma thiopentone concentrations of 50 ng/ml, 4.8 μg/ml and 60 μg/ml, respectively. The coefficient of variation for the assay of ultrafiltrates was 2.6 percent ($n = 4$) at 60 ng/ml.

The plasma protein binding of thiopentone was determined using the Micropartition System MPS-1 (Amicon Corporation, U.S.A.). Plasma (0.5 ml) was filtered in an atmosphere of 5 percent carbon dioxide in oxygen at 37°C for 20 minutes, which yielded 0.25–0.30 ml of ultrafiltrate. After verifying the absence of protein (Albustix, Ames) ultrafiltrates were assayed for thiopentone using the method described for plasma. The unbound fraction of thiopentone was taken as the ratio ultrafiltrate concentration/concentration in an aliquot of unfiltered plasma. Control experiments, in which previously prepared ultrafiltrates spiked with thiopentone (0.09 μg/ml) were subjected to ultrafiltration, demonstrated negligible loss of drug to the apparatus during the filtration process. The coefficient of variation of the method from replicate determinations of unbound fraction on a single plasma pool was 2.5 percent ($n = 5$) at a plasma concentration of 22.7 μg/ml. The plasma albumin concentration was determined by radial immunodiffusion using M-Partigen albumin plates (Behringwerke, AG). Data are presented as mean and standard deviations. Correlation between variables were investigated by linear regression and differences among means of two or more groups of dependent data by the Bonferroni t-test[21] assuming normally distributed data. A probability value of less than 0.05 was considered statistically significant.

Results

The infusion pattern, and the profiles of total and unbound thiopentone concentration of one of the patients during surgery are shown in Fig. 1.

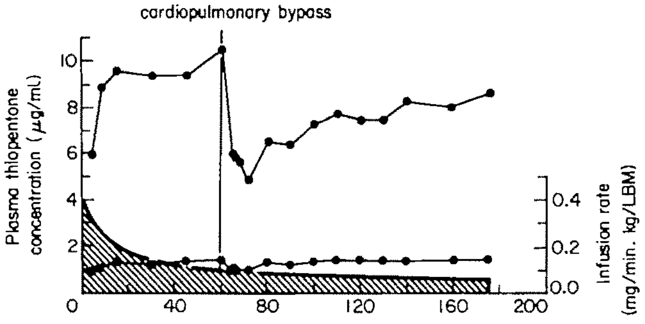


Fig. 1. Plasma total and unbound thiopentone concentrations (left-hand scale) during exponential infusion of thiopentone (hatched area, right-hand scale) for cardiac surgery for patient 5. The initial bolus dose was 1.79 mg/kg LBM.

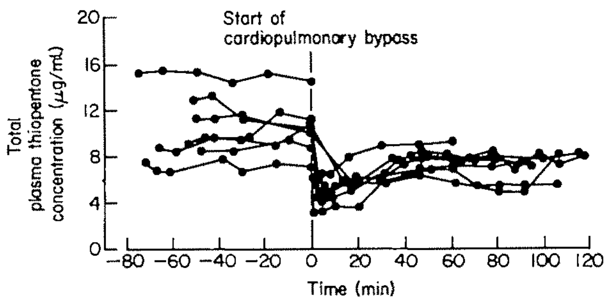


Fig. 2. Total plasma thiopentone concentrations during continuous infusion. The point of reference (zero time) is taken as the start of bypass.

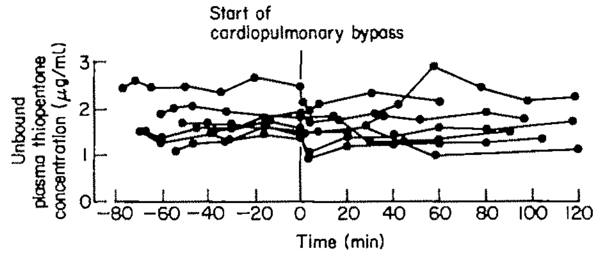


Fig. 3. Unbound (free) plasma thiopentone concentrations during continuous infusion. The point of reference (zero time) is taken as the start of bypass.

Figure 2 shows the profiles for total thiopentone for all seven patients. With the exception of patient seven, in whom the thiopentone infusion was not commenced until 8 minutes after the bolus dose, the profile of total plasma thiopentone was relatively stable prior to the onset of bypass. Immediately prior to bypass, the mean total plasma thiopentone concentration was 10.2 (SD 2.1) μg/ml, some two thirds of that predicted from averaged pharmacokinetic data. At the onset of bypass, there was an abrupt decline in total plasma thiopentone concentration to 4.90 (SD 1.14) μg/ml, which was 50.0 (SD 5.8) percent of the prebypass level. Plasma concentrations then rose gradually and reached a new plateau of 6.99 (SD 1.38) μg/ml, which was 70 (SD 8.8) per cent of the prebypass level.

The profiles of plasma concentration of unbound thiopentone during surgery are shown in Fig. 3. Shortly before the onset of bypass, the mean plasma concentration of unbound thiopentone was 1.69 (SD 0.38) μg/ml. Following the onset of bypass, there was a smaller decline in plasma concentrations of unbound thiopentone, which fell to 1.29 (SD 0.39) μg/ml, which was 76.4 (SD 15.7) percent of the prebypass level. Unbound levels then increased more rapidly than total levels, such that at the end of bypass, mean unbound concentration was 1.62 (SD 0.43) μg/ml, which was similar to the prebypass unbound level.

The mean unbound fraction of thiopentone in plasma was 16.6 (SD 1.9) percent before bypass, increased significantly to 29.3 (SD 5.6) percent shortly after the onset of bypass and was still elevated at the end of bypass (22.9, SD 3.3 percent), and 5–7 h after cessation of bypass (20.5, SD 2.5, percent, Table 2). During bypass, haematocrit fell from 0.44 (SD 0.02) to 0.25 (SD 0.03), due to haemodilution by the pump priming solution. In a separate study, the mean unbound fraction of thiopentone in the pump priming solution (albumin concentration 20.8 g/litre) was 52.8 (SD 1.2) percent ($n = 3$) at a thiopentone concentration of 7.45 μg/ml. In plasma samples taken before, during and 5–7 hours after bypass, the plasma albumin concentrations were 36.2 (SD 2.5) g/litre 27.7 (SD 2.4) g/litre and 36.1 (SD

Table 2. Plasma protein binding of thiopentone before, during and after bypass

Subject	Percent thiopentone unbound Before bypass	Maximum during bypass	At cessation of bypass	After bypass
1	15.1	26.4	23.3	21.3
2	17.2	32.1	21.3	21.4
3	16.7	39.1	27.7	23.3
4	19.4	29.5	22.2	22.5
5	13.3	20.7	17.1	16.3
6	17.6	29.1	25.4	20.6
7	16.8	28.3	23.0	17.8
Mean	16.6	29.3*	22.9*†	20.5*†
SD	1.9	5.6	3.3	2.5

*Significantly greater than prebypass value ($p<0.01$).
†Significantly less than maximum during bypass ($p<0.01$).

4.0) g/litre, respectively. There was a strong correlation between the binding ratio of thiopentone (ratio of plasma bound fraction/unbound fraction[22]) and the plasma albumin concentration ($r=0.69$, $p<0.001$, $n=28$) before and after bypass. This suggests that the decrease in plasma binding during bypass was due largely to haemodilution.

Discussion

The combination of an induction bolus dose and an exponentially decreasing infusion of thiopentone was successful in maintaining plasma thiopentone concentrations relatively constant up until the onset of bypass (Fig. 2). The average level achieved, however, was somewhat lower than that expected and of a similar order to that reported in a previous study.[20] Possible reasons for the departure from the desired level may relate to the mean LBM of 55 kg assumed for the previous studies, differences in the sex distribution between different studies or to the relatively small data base available for the generation of the averaged pharmacokinetic constants. A further possibility is that some real difference exists in both distribution and clearance of thiopentone between the conditions during infusion and the hours following dosage where single dose kinetic parameters are derived.

At the onset of bypass, total plasma thiopentone concentration fell abruptly by about half. The fall in haematocrit was of the same order, suggesting that haemodilution was the cause of the fall in total thiopentone levels. Haemodilution also appeared to cause a decrease in plasma protein binding of thiopentone during bypass. Unbound fraction of thiopentone increased from 16.6 (SD 1.9) percent before bypass to a maximum of 29.3 (SD 5.6) percent during bypass (Table 2). An increase in plasma nonesterified fatty acid (NEFA) concentration *in vitro* following heparin administration to the patient has been shown to cause an artefactual decrease in protein binding of certain drugs in plasma collected during bypass.[23,24] It is unlikely that this caused the decrease in thiopentone binding because collection of blood in ice and the short duration of ultrafiltration (20 minutes) minimise *in vitro* NEFA formation.[23,24] Furthermore, thiopentone binding in plasma is not altered by the *in vitro* addition of NEFA.[25] On the other hand, there was a strong correlation between the binding ratio of thiopentone and the plasma albumin concentration, and the binding of thiopentone in the pump priming solution was low (52.8, SD 1.2, percent unbound). As discussed by Nielsen *et al.*,[22] the extent of the drug–protein interaction, as given by the ratio of the bound concentration (B) to the free concentration (F), depends on the number of binding sites (n), the protein concentration (P), the dissociation constant of the binding (K_D) and the free drug concentration according to:

$$\frac{B}{F}=\frac{nP}{K_D+F} \tag{4}$$

From this equation,[22] it is clear that the extent of drug-protein binding is related to P and that the relationship is linear when K_D is much greater than F, as it is in this case. The binding would therefore be expected to decrease with a decrease in plasma protein concentration. This confirms that the main cause of the low binding of thiopenton during bypass was haemodilution.

At the onset of bypass, the unbound plasma thiopentone also decreased (Fig. 3), but the decrease was smaller than that with total thiopentone, probably because of the compensatory effect of the concomitant increase in unbound fraction of drug in plasma. During bypass, the total thiopentone level rose gradually, but did not reach the prebypass level by the end of the infusion. The decrease in unbound thiopentone level was more transient, however, as the prebypass level was reached by the end of bypass.

The onset of cardiopulmonary bypass has been found to affect plasma drug concentrations in a variety of ways, depending on the particular drug. With several of the muscle relaxants, plasma concentrations of both total and unbound drug increase at the onset of bypass, and dosage requirements decrease, possibly due to contraction in blood volume or decreased tissue perfusion.[2-4] Conversely, total plasma concentrations of a variety of other drugs have shown about a 50 percent decrease at the onset of bypass, presumably due to haemodilution.[5-12] Apparent slow elimination of some drugs during and/or after bypass has been explained in terms of a reduction in renal excretion,[9] or a reduction in metabolic clearance due to either decreased hepatic blood flow[5-7] or hypothermia.[7,8] However, most of these studies failed to measure plasma concentrations of unbound drug, used a single bolus dose rather than continuous administration and used kinetic parameters derived from data extending over the entire operative period. Such limitations compromise the accuracy of the conclusions from these studies.

In the present study, the effect of bypass on thiopentone plasma concentrations was investigated under essentially steady-state conditions. Thiopentone is eliminated mainly by hepatic metabolism,[26] and its hepatic extraction ratio[17] is of the same order as the unbound fraction of the drug in plasma (Table 2). Thiopentone may therefore be classified as a member of the capacity-limited restrictively cleared group of drugs.[27] Following a decrease in binding of such a drug, steady-state total drug levels will fall but, apart from some initial fluctuations, the steady-state unbound drug concentration will remain relatively unchanged. This has been illustrated well in a study of the displacement of bilirubin from plasma proteins by sulfisoxazole in rats.[28] The relatively prompt return of the unbound thiopentone level to the prebypass value is consistent with this predicted behaviour. The unchanged unbound level also implies that the intrinsic, or unbound clearance of thiopentone remained unchanged throughout surgery. As it is the unbound moiety that is pharmacologically active, the thiopentone dosage requirements should not change during bypass, provided the relationship between unbound concentration and anaesthetic effect remains constant.

In conclusion, this study shows that changes in thiopentone plasma binding during cardiopulmonary bypass compensate for considerable haemodilution and, as a result, the unbound concentration of thiopentone is unaffected. Thus, a preprogrammed exponentially decaying thiopentone infusion may be a suitable anaesthetic technique for cardiac surgical patients, on the grounds that a steady concentration of the active fraction of the primarily hypnotic agent is maintained throughout the period of administration.

Acknowledgments

The work was supported by grants from the George Hicks Foundation, Travenol Laboratories Pty. Ltd. and the National Health and Medical Research Council of Australia.

References

1. Holley FO, Ponganis KV, Stanski DR. Effect of cardiopulmonary bypass on the pharmacokinetics of drugs. *Clinical Pharmacokinetics* 1982; **7:** 234–51.
2. Shanks CA, Ramzan IM, Walker JS, Brown KF. Gallamine disposition in open-heart surgery involving cardiopulmonary bypass. *Clinical Pharmacology and Therapeutics* 1983; **33:** 792–9.
3. Walker JS, Brown KF, Shanks CA. Alcuronium kinetics in patients undergoing cardiopulmonary bypass surgery. *British Journal of Clinical Pharmacology* 1983; **15:** 237–44.
4. Walker JS, Shanks CA, Brown KF. Altered d-tubocurarine disposition during cardiopulmonary bypass surgery. *Clinical Pharmacology and Therapeutics* 1984; **35:** 686–94.
5. Plachetka JR, Salomon NW, Copeland JG. Plasma propranolol before, during, and after cardiopulmonary bypass. *Clinical Pharmacology and Therapeutics* 1981; **30:** 745–51.
6. Koska AJ, Romagnoli A, Kramer WG. Effect of cardiopulmonary bypass on fentanyl distribution and elimination. *Clinical Pharmacology and Therapeutics* 1981; **29:** 100–5.

7. Bentley JB, Cork RC. Fentanyl sequestration in lungs during cardiopulmonary bypass. *Clinical Pharmacology and Therapeutics* 1983; **34:** 703–6.
8. Miller KW, Conahan TJ, Chan KKH, McCoy HG, Fischer RP, Lindsay WG, Zaske DE. Cephalothin kinetics: before, during and after cardiopulmonary bypass surgery. *Clinical Pharmacology and Therapeutics* 1979; **26:** 54–62.
9. Miller KW, McCoy HG, Chan KKH, Fischer RP, Lindsay WG, Seifert RD, Zaske DE. Effect of cardiopulmonary bypass on cefazolin disposition. *Clinical Pharmacology and Therapeutics* 1980; **27:** 550–6.
10. Storstein L, Nitter-Hauge S, Fjeld N. Effect of cardiopulmonary bypass with heparin administration on digitoxin pharmacokinetics, serum electrolytes, free fatty acids, and renal function. *Journal of Cardiovascular Pharmacology* 1979; **1:** 191–204.
11. Morrell DF, Harrison GG. Lignocaine kinetics during cardiopulmonary bypass. Optimum dosage and the effects of haemodilution. *British Journal of Anaesthesia* 1983; **55:** 1173–7.
12. D'Hollander AA, Duvaldestin P, Henzel D, Nevelsteen M, Bomblet JP. Variations in pancuronium requirement, plasma concentration, and urinary excretion induced by cardiopulmonary bypass with hypothermia. *Anesthesiology* 1983; **58:** 505–9.
13. Kruger-Thiemer E. Continuous intravenous infusion and multicompartment accumulation. *European Journal of Pharmacology* 1968; **4:** 317–24.
14. Gibaldi M, Perrier D. *Pharmacokinetics*. New York: Marcel Dekker, 1982.
15. Christensen JH, Andreasen F, Jansen JA. Pharmacokinetics of thiopentone in a group of young women and a group of young men. *British Journal of Anaesthesia* 1980; **52:** 913–7.
16. Christensen JH, Andreasen F, Jansen J. Pharmacokinetics and pharmacodynamics of thiopental in patients undergoing renal transplantation. *Acta Anaesthesiologica Scandinavica* 1983; **27:** 513–8.
17. Morgan DJ, Blackman GL, Paull JD, Wolf LJ. Pharmacokinetics and plasma binding of thiopental. 1. Studies in surgical patients. *Anesthesiology* 1981; **54:** 468–73.
18. Jung D, Mayersohn M, Perrier D, Calkins J, Saunders R. Thiopental disposition in lean and obese patients undergoing surgery. *Anesthesiology* 1982; **56:** 269–74.
19. Wulfsohn NL, Joshi CW. Thiopentone dosage based on lean body mass. *British Journal of Anaesthesia* 1969; **41:** 516–21.
20. Crankshaw DP, Edwards NE, Blackman GL, Boyd MD, Chan HNJ, Morgan DJ. Evaluation of infusion regimens for thiopentone as a primary anaesthetic agent. *European Journal of Clinical Pharmacology* 1985; **28:** 543–52.
21. Miller RG. *Simultaneous statistical inference*. New York: McGraw-Hill, 1966.
22. Nilsen OG, Leren P, Aakesson I, Jacobsen S. Binding of quinidine in sera with different levels of triglycerides, cholesterol, and orosomucoid protein. *Biochemical Pharmacology* 1978; **27:** 871–6.
23. Giacomini KM, Sweazey SE, Giacomini JC, Giacomini TF. Administration of heparin causes *in vitro* release of non-esterified fatty acids in human plasma. *Life Sciences* 1980; **27:** 771–80.
24. Brown JE, Kitchell BB, Bjornsson TD, Shand DG. The artifactual nature of heparin-induced drug protein-binding alterations. *Clinical Pharmacology and Therapeutics* 1981; **30:** 636–43.
25. Morgan DJ, Toh CT, Blackman GL, Paull JD. Plasma binding of thiopentone in late pregnancy. *British Journal of Clinical Pharmacology* 1983; **15:** 121–2.
26. Dundee JW. Biotransformation of thiopentone and other thiobarbiturates. *International Anesthesiology Clinics* 1974; **12:** 121–33.
27. Wilkinson GR, Shand DG. A physiological approach to hepatic drug clearance. *Clinical Pharmacology and Therapeutics* 1975; **18:** 377–90.
28. Oie S, Levy G. Effect of sulfisoxazole on pharmacokinetics of free and plasma protein-bound bilirubin in experimental unconjugated hyperbilirubinemia. *Journal of Pharmaceutical Sciences* 1979; **68:** 6–9.

Anaesthesia, 1986, Volume 41, pages 11–15

C-reactive protein in patients undergoing cardiac surgery

H. BORALESSA, F. C. DE BEER, A. MANCHIE, J. G. WHITWAM
AND M. B. PEPYS

Summary

Among 25 patients undergoing cardiac surgery with the aid of cardiopulmonary bypass, 13 who recovered uneventfully all had normal (< 2 mg/litre) levels of serum C-reactive protein pre-operatively. In contrast, 10 of the 12 patients who suffered from various postoperative complications, including two who died, had abnormally raised levels of C-reactive protein pre-operatively. All patients showed a major acute phase response to surgery with peak C-reactive protein levels at about 46 hours but, whereas the uncomplicated cases showed a characteristic smooth biphasic pattern of declining levels thereafter, the complicated cases all exhibited significant alterations of this pattern. The occurrence during the postoperative period of a secondary rise in C-reactive protein or the failure of the level to continue falling, generally preceded clinical evidence of intercurrent infection. Pre-operative measurement of serum C-reactive protein may thus make a valuable contribution to the assessment of patients requiring elective cardiac surgery; regular post-operative monitoring can provide early warning of serious complications.

Key words

Surgery; cardiopulmonary bypass.
Allergy; C-reactive protein.

Cardiac surgery with cardiopulmonary bypass is a major procedure, usually performed electively, following which there is a significant incidence of serious complications, including pulmonary collapse, bacterial infections, myocardial infarction and pulmonary embolism.[1,2] The management of such patients would be improved if it were possible to identify pre-operatively those individuals in whom the risks of a postoperative complication were greater, and if the occurrence of such complications could be recognised as early as possible.

C-reactive protein is the classical acute phase protein; its circulating concentration increases from trace levels in healthy subjects, in response to most forms of tissue injury, infection and inflammation.[3–5] This non-specific response of the C-reactive protein concentration may occur very rapidly, and increases from normal to over a thousand-fold are seen within 24–48 hours of an acute stimulus, such as a major surgical operation. With prompt resolution of a stimulus, such as effective therapy of a microbial infection, the level may fall equally rapidly.[3–5]

H. Boralessa, FFARCS, Senior Registrar, Department of Anaesthesia, F.C. de Beer, MRCP, Research Fellow, Immunological Medicine Unit, A. Manche, MB, BS, Senior House Officer, Department of Surgery, J.G. Whitwam, FFARCS, Professor of Clinical Anaesthesia, Department of Anaesthetics, M.B. Pepys, FRCP, Professor, Immunological Medicine Unit, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 OHS.

0003–2409/86/010011 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

We have therefore investigated the possible role of frequent sequential measurement of the serum concentration of C-reactive protein in the management of patients undergoing cardiac surgery with cardiopulmonary bypass.

Methods

Thirteen male and twelve female patients undergoing coronary artery or valvular surgery with standard anaesthetic, operative and bypass procedures, were studied. Pre-operative diagnoses and identification of postoperative complications were established by standard clinical, microbiological and other laboratory tests and criteria. Venous blood samples were taken pre-operatively, immediately after surgery and approximately 12 hourly each day until discharge from hospital. In ten patients, samples were also taken immediately after induction of anaesthesia, after heparinisation, and at 10, 20, 30 and 60 minutes after commencement of cardiopulmonary bypass. The blood was allowed to clot at room temperature for 1 hour before separation of serum which was stored frozen at −20°C.

The C-reactive protein concentration was measured in an electro-immunoassay which was calibrated with standards of isolated pure protein and had a coefficient of variation of replicate assays of less than 10%.[6,7] The lower limit of sensitivity of the assay was 2 mg/litre; 90% of normal healthy subjects have levels less than 3

Table 1. Postoperative complications following cardiac surgery

Patient	Diagnosis	Pre-operative serum C-reactive protein concentration (mg/litre)	Procedure	Complication
1	Aortic stenosis	35	Aortic valve replacement	Intra-operative death
2	Mitral valve disease	26	Mitral valve replacement	*E. coli* pneumonia
3	Subacute bacterial endocarditis on prosthetic mitral valve	9	Mitral valve replacement	*Pseudomonas* pneumonia
4	Eosinophilic myocarditis	28	Mitral valve replacement	Cardiac failure Pulmonary oedema
5	Marfan's syndrome Severe biventricular failure	116	Aortic valve replacement	Pulmonary infarction
6	Aortic stenosis	11	Aortic valve replacement	*Enterobacter* pneumonia Wound infection
7	Aortic stenosis	4	Aortic valve replacement	*Enterobacter* pneumonia
8	Eosinophilic myocarditis	4	Aortic valve replacement	Pneumonia
9	Mitral valve disease. Previous mitral valve replacement 7 days earlier	162	Repair of paraprosthetic leak	Pneumonia and urinary infection with *Pseudomonas*
10	Aortic stenosis	74	Emergency aortic valve replacement	Myocardial splenic and pulmonary infarction. Bronchopneumonia. Death day 7.
11	Coronary atherosclerosis	2	Coronary artery bypass graft	Peri-operative myocardial infarction. Sudden death day 12 without fresh infarction.
12	Coronary atherosclerosis	2	Coronary artery bypass graft	Pneumonia

mg/litre and 99% have less than 10 mg/litre.[8] Although the samples were collected prospectively, the assays were performed in batches, after the clinical study was completed. The serum values do not fall within a normal distribution and the significance of differences between maximum levels at different intervals and in different groups was therefore sought using Wilcoxon's rank sum test.

Results

Thirteen of the patients studied recovered uneventfully and were discharged from hospital 9–10 days after operation. The other 12, however, all suffered some form of complication which resulted in death in 3 cases and, in the remainder, necessitated a more prolonged stay in either the intensive care unit, the convalescent ward or both. The pre-operative C-reactive protein values in these two groups of patients were significantly different. All the patients who recovered without incident had normal levels of < 2 mg/litre, but ten of the twelve who developed complications had raised levels (Table 1), including one who had had a mitral valve replacement 7 days before the operation to repair a paraprosthetic leak.

Three individuals died during the study period. One was a 69-year-old woman undergoing emergency aortic valve replacement whose pre-operative C-reactive protein was 74 mg/litre, and who died 7 days later. Autopsy revealed a week old myocardial infarct, bronchopneumonia, splenic and pulmonary infarcts. The second was a 65-year-old woman with a level of 34 mg/litre, who was in a low output state pre-operatively and who died during an emergency coronary artery bypass operation for unstable angina. The third was a 52-year-old man whose pre-operative C-reactive protein was 2 mg/litre, but who suffered a peri-operative myocardial infarction from which he apparently made a good recovery. However, he died suddenly on day 12. No other cause of death was found at autopsy.

No immediate increase of C-reactive protein concentration was seen following induction of anaesthesia or the institution of cardiopulmonary bypass in the 10 patients in whom early samples were taken. However, as expected, there were major postoperative rises in all the patients with the peak at a mean of 46 hours (SD 12 hours) after surgery. Among the 13 patients who recovered uninterruptedly, there was a biphasic decline in the protein levels (Fig. 1). There was an early rapid fall from a median value of 232 mg/litre at the peak to a median of 75 mg/litre at 5 days, followed by a more gradual reduction, continuing smoothly through a median of 42 mg/litre at 7 days until the patients were discharged after 10 days. Two patients in this group had episodes of chest pain and 2 others developed dysrhythmias requiring cardioversion, but there was no C-reactive protein response to these events and they did not affect the patients' general clinical condition.

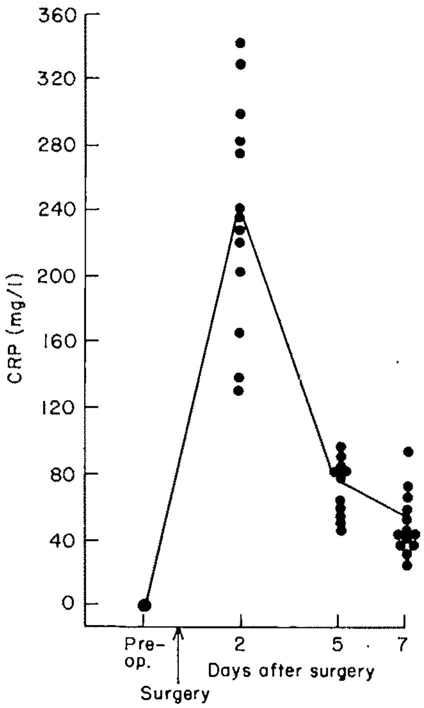


Fig. 1. Serum C-reactive protein concentration in individuals undergoing cardiac surgery in whom there was an uneventful postoperative course. Each point represents a single estimation in an individual patient. All patients had normal levels (2 mg/l) pre-operatively. The lines join the median values at each interval. CRP, C-reactive protein.

The peak levels attained in the group who subsequently developed complications (median 208 mg/litre) were not significantly different from those in the uncomplicated group; however, there was a marked difference in the subsequent pattern (Fig. 2). The median value was higher at 99 mg/litre on day 5 ($p < 0.05$) and remained at 100 mg/litre on day 7 ($p < 0.01$). These distortions in the normal course of the acute phase response

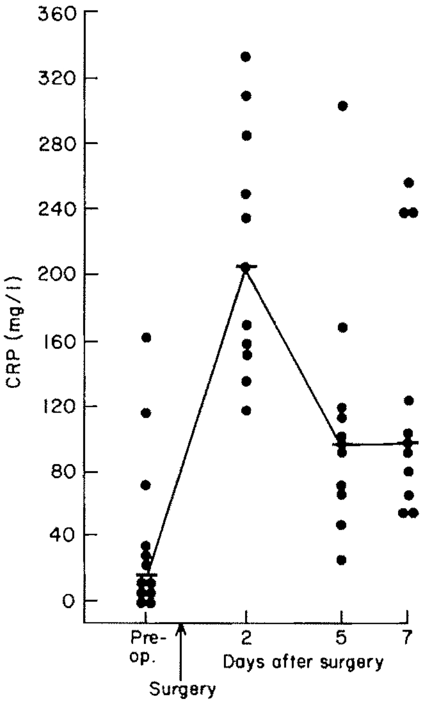


Fig. 2. Serum C-reactive protein concentration in individuals undergoing cardiac surgery in whom there was a complicated postoperative course. Each point represents a single estimation in an individual patient. The lines join the median values at each interval. CRP, C-reactive protein.

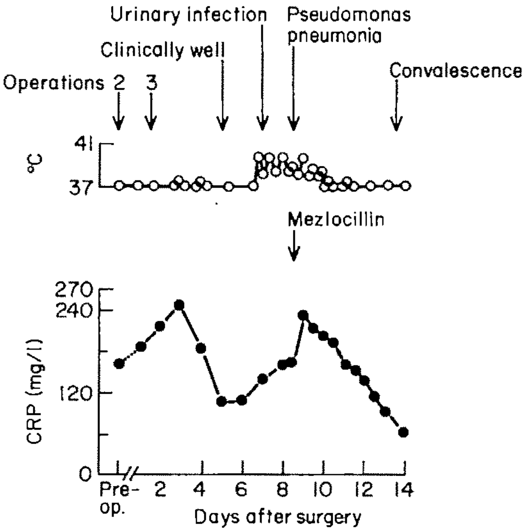


Fig. 3. Serum C-reactive protein response to serious postoperative infection in patient 9 who underwent two operations for repair of paraprosthetic leakage following mitral valve replacement. CRP, C-reactive protein.

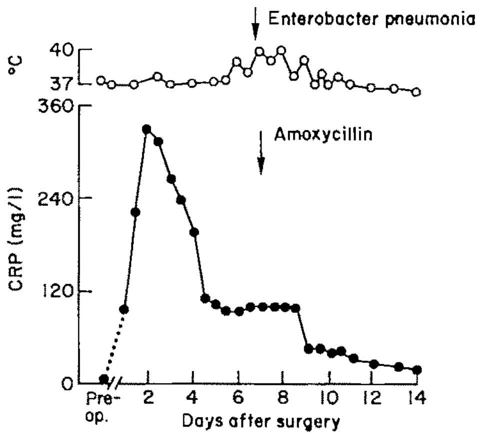


Fig. 4. Serum C-reactive protein response to bacterial infection of low virulence following elective aortic valve replacement (patient 7). CRP, C-reactive protein.

to surgery were due either to secondary elevations in the C-reactive protein level in patients who suffered serious bacterial infections, for example with *Pseudomonas*, (Fig. 3), or in whom myocardial or pulmonary infarction occurred, or a failure of the fall in levels to be maintained, as in patients who were infected with less virulent organisms such as *Enterobacter* (Fig. 4). It was notable that, in both cases, the change in C-reactive protein response, that is the failure of levels to continue falling or the occurrence of a secondary rise, generally preceded clinical evidence of the causative complication by as much as 24 hours (Figs 3,4).

Discussion

The present results confirm other work[2,9,10] on the patterns of serum C-reactive protein response to surgery and postoperative complications, and they significantly extend it by virtue of the use of frequent measurements in closely monitored patients, thus establishing that aberrations in the normal postoperative pattern can predict infective complications. These findings, together with the increasing availability of commercial assay systems capable of providing a precise serum C-reactive protein value within 1–2 hours of sampling, might lead to more widespread application of this test in patients undergoing cardiac surgery and also other forms of major surgery. The information yielded by the response is non-specific, but its great sensitivity can nonetheless trigger active clinical investigation and management, which may be of critical importance in these high risk patients.

A novel finding which emerged from our study, was that an abnormal serum C-reactive protein pre-operatively predicted a complicated post-operative course. Confirmation of this is currently being sought by a more extensive investigation now in progress. The implication is that any on-going organic disease process of sufficient severity to cause elevation of the serum C-reactive protein concentration may be likely to prejudice the patient's capacity to withstand the major stresses involved in cardiac surgery. It would therefore seem prudent to measure the serum level pre-operatively, a very simple, inexpensive and objective procedure, in all cases of elective major surgery. If it is found to be raised, then the cause should, if possible, be identified and eliminated before proceeding. Clearly this suggestion is not appropriate when the cause of the raised C-reactive protein is itself the indication for surgery, but this is not the case in patients undergoing elective coronary artery bypass surgery or valve replacement.

Acknowledgments

We thank Professor H.H. Bentall and Mr R.N. Sapsford for permission to study their patients. This work was supported in part by MRC Programme Grant G979/51 to MBP.

References

1. Gale GD, Teasdale SJ, Sanders DE, Bradwell PJ, Russell A, Solarik B, York JE. Pulmonary atelectasis and other respiratory complications after cardiopulmonary bypass and investigation of aetiological factors. *Canadian Anaesthetists' Society Journal* 1979; **26:** 15–21.
2. Ghoneim ATM, McGoldrick J, Ionescu MI. Serial C-reactive protein measurements in infective complications following cardiac operation: evaluation and use in monitoring response to therapy. *Annals of Thoracic Surgery* 1982; **34:** 166–75.
3. Kushner I, Volanakis JE, Gewurz H (eds). C-reactive protein and the plasma protein response to tissue injury. *New York Annals of the Academy of Science* 1982; 389.
4. Pepys MB. C-reactive protein fifty years on. *Lancet* 1981; **1:** 653–6.
5. Pepys MB, Baltz ML. Acute phase proteins with special reference to C-reactive protein and related proteins (pentaxins) and serum amyloid A protein. In: Dixon FJ, Kunkel HG, eds. *Advances in immunology*, 34. New York: Academic Press, 1983.
6. Pepys MB, Dash AC, Markham RE, Thomas HC, Williams BD, Petrie A. Comparative clinical study of protein SAP (amyloid P component) and C-reactive protein in serum. *Clinical and Experimental Immunology* 1978; **32:** 119–24.
7. de Beer FC, Pepys MB. Isolation of human C-reactive protein and serum amyloid P component. *Journal of Immunological Methods* 1982; **50:** 17–31.
8. Shine D, de Beer FC, Pepys MB. Solid phase radioimmunoassays for C-reactive protein. *Clinical Chimica Acta* 1981; **117:** 13–23.
9. Fischer CL, Gill C, Forrester MG, Nakamura R. Quantitation of 'acute-phase proteins' post-operatively. Value in detection and monitoring complications. *American Journal of Clinical Pathology* 1976; **66:** 840–6.
10. Pelissier E, Audouy JP, Mercadier A, Collon L, Jaulmes B. Dosage de la protéine C réactive (CRP). Intérêt au décours de la chirurgie cardiovasculaire sous circulation extracorporelle. *Nouvelle Press Medicale* 1981; **10:** 3247.

Anaesthesia, 1986, Volume 41, pages 16–20

Transdermal hyoscine and postoperative nausea and vomiting

J. UPPINGTON, J. DUNNET AND C. E. BLOGG

Summary

Forty-two patients, undergoing major gynaecological surgery, were randomly allocated to have a patch applied to the skin behind one ear, containing either hyoscine or placebo. They were followed up at 24-hour intervals for 3 days postoperatively and divided into matched pairs for statistical analysis. There was a significant ($p < 0.01$) reduction in nausea and vomiting in the first 24 hours postoperatively, but no difference thereafter. There was an increased incidence of visual disturbance in the hyoscine group at 48 hours, but no other differences in the side effects studied at any other time. However, despite receiving hyoscine there was still a high incidence (68%) of severe nausea and vomiting.

Key words

Anaesthesia; complications; postoperative vomiting.
Antiemetics; hyoscine.

Nausea and vomiting are distressing and frequent complications of anaesthesia and surgery. There may have been a reduction in the severity of the symptoms over the years, but the reported incidence probably has not changed very much, and is of the order of 20–40% of all cases.[1]

Anaesthesia is noted for the multiplicity of routes used for drug administration, ranging from inhalational to intravenous. Until recently, the transdermal route, for systemic rather than local effect, was only available for nitroglycerine. This route has several potential advantages in terms of patient acceptability and drug delivery and it should be possible to maintain constant drug levels over a long period of time. An effective preparation of hyoscine, for prevention of motion sickness,[2,3] that is absorbed through the skin (Transderm Scop, ALZA Corporation), is now available in the United States and continental Europe. This study was designed to evaluate the use of transcutaneous hyoscine in the prevention of postoperative nausea and vomiting.

Materials and methods

The transcutaneous hyoscine system consists of a small circular film, 2.5 sq cm in area and 18 mm in diameter, containing four layers laminated together.[4] These are, from the outside in, an impermeable flesh-coloured surface, a reservoir of drug containing inactive mineral oil (12.5 mg), polyisobutylene (11.4 mg) and active hyoscine (1.5 mg, of which 0.5 mg is delivered over 3 days), a microporous rate-controlling polypropylene membrane, and an adhesive which contains a small quantity of hyoscine for immediate release. The

---

J. Uppington, MB, BS, FFARCS, Senior Registrar, J. Dunnet, MB, ChB, FFARCS, Registrar, C.E. Blogg, MB, BS, FFARCS, Consultant and Clinical Lecturer, Nuffield Department of Anaesthetics, Radcliffe Infirmary, Oxford, OX2 0HE.

0003-2409/86/010016 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

system is based on a kinetic model that has been confirmed experimentally.[5] Release of the drug occurs by diffusion from the reservoir through the rate-controlling membrane and adhesive, to the skin surface (which can absorb the drug at many times the rate that it is released by the system). The skin behind the ear has suitable characteristics for the transdermal absorption of hyoscine.

Forty-two adult women, undergoing major gynaecological surgery, were studied. All were ASA class I and II, and aged between 18 and 65 years. The operations were vaginal or abdominal hysterectomy, oophorectomy or tubal surgery. Approval for the study was obtained from the Central Oxford Research Ethics Committee, and signed informed consent was obtained from each patient prior to entering the trial.

Each patient was seen pre-operatively by one of the authors, and randomly allocated to receive either a transdermal hyoscine patch (Transderm Scop, ALZA Corp.) or placebo. This was placed behind the ear on the evening prior to surgery. The placebo was a Band-aid patch (Johnson and Johnson) and each hyoscine patch was covered by a similar Band-aid for protection and so that its identity could not be distinguished from placebo by patient or assessor.

Premedication was with diazepam 10 mg orally, approximately 2 hours prior to induction of anaesthesia. Anaesthesia was induced with thiopentone (4–5 mg/kg) and maintained with halothane or enflurane (0.5–1%) with 66% nitrous oxide in oxygen, 3–5 μg/kg of fentanyl and a non-depolarising relaxant. The residual effects of the muscle relaxants were reversed with standard doses of atropine and neostigmine. Fluid loss was replaced with Hartmann's solution at a rate of 5–10 ml/kg/hour, and blood was transfused as clinically indicated. No patient was given prophylactic anti-emetics pre- or intra-operatively.

The patients had previously been told they could receive anti-emetics if they asked for them and the nurses were instructed only to give anti-emetics when the patient requested them. All patients were prescribed 15–20 mg of papaveretum intramuscularly, up to 2-hourly, as required and 10 mg of intramuscular metoclopramide, up to 4-hourly, when requested. If more than three or four doses of metoclopramide were needed, the nurses were given the option to switch to intramuscular prochlorperazine 12.5 mg 4-hourly, as required.

The patients were visited 24, 48 and 72 hours postoperatively by an author who had not seen them pre-operatively and who had not been told which medication they had been given. Enquiries were made as to the amount of nausea and vomiting the patients had experienced during the preceding 24 hours and scored as 0 = no nausea or vomiting, 1 = mild nausea (feeling nauseated but not severe enough to want an anti-emetic), 2 = severe nausea (wanting an anti-emetic), 3 = vomiting. Retching was equated with vomiting. In addition, the incidence of dry mouth, pre- and postoperatively, and visual disturbance was noted as 0 = absent, 1 = present. The number of doses of anti-emetic or analgesic were noted for each postoperative period.

The patients were then arranged as a series of matched pairs. The factors that were particularly matched were previous surgery or not, presence or absence of nausea and vomiting following previous anaesthesia and surgery, whether the patients suffered from travel sickness or not, and as far as possible, patients were matched by weight and type of surgery.

Statistical analysis of the data was carried out by the Wilcoxon matched-pairs signed-rank test (for nausea/vomiting scores and drug dosage), the sign test (for side effects) and *t*-test with correlations (for the demographic data).

Results

Of the 42 patients who started the trial, four were withdrawn. Three of these received non-standard anaesthetics (extradural or spinal block), two in the hyoscine group and one in the placebo group. The other patient who was withdrawn was in the placebo group, and had been given metoclopramide prior to induction. Thus, data on 38 patients were completed.

The mean values (SD) for age were 39.9 (7.1) and 39.3 (6.3) years in the hyoscine and placebo groups respectively. The respective weights were 65.9 (6.9) and 64.6 (10.7) kg. These differences were not statistically significant.

The scores for nausea and vomiting in the groups of paired data for the separate periods of the first, second and third 24 hours postoperatively, are given in Table 1. There was a significant reduction in score on the first postoperative day ($p < 0.01$), for those pairs receiving hyoscine. No significant differences occurred on the second day.

Table 1. Nausea and vomiting score

Pair Number	First 24 hours		Second 24 hours		Third 24 hours	
	Hyoscine	Placebo	Hyoscine	Placebo	Hyoscine	Placebo
1	3	3	1	0	0	0
2	2	3	2	0	0	0
3	0	2	0	1	0	0
4	3	3	0	0	0	0
5	2	2	2	2	0	0
6	0	3	0	3	0	0
7	3	3	2	3	0	3
8	2	3	3	1	1	0
9	3	3	0	2	0	0
10	3	3	0	2	0	0
11	0	2	0	3	0	0
12	2	3	2	0	0	0
13	2	2	1	2	0	0
14	0	3	0	0	0	0
15	0	2	0	1	0	0
16	3	2	3	0	3	0
17	1	3	2	1	0	0
18	3	3	0	1	0	0
19	3	3	2	3	0	1

0 = no nausea or vomiting; 1 = mild nausea; 2 = severe nausea; 3 = vomiting.

Table 2. Incidence of nausea and vomiting. Number of patients (percentage). 19 patients in each group

	First 24 hours		Second 24 hours		Third 24 hours	
	Placebo	Hyoscine	Placebo	Hyoscine	Placebo	Hyoscine
Vomiting	13 (68)	8 (42)	4 (21)	2 (11)	1 (5)	1 (5)
Severe nausea	6 (32)	5 (26)	4 (21)	6 (32)	0 (0)	0 (0)
Mild nausea	0 (0)	1 (5)	5 (26)	2 (11)	1 (5)	1 (5)
No nausea	0 (0)	5 (26)	6 (32)	9 (47)	17 (90)	17 (90)

Table 3. Numbers of patients experiencing side effects. Number of patients (percentage). 19 patients in each group

	First 24 hours		Second 24 hours		Third 24 hours	
	Placebo	Hyoscine	Placebo	Hyoscine	Placebo	Hyoscine
Pre-operative dry mouth	9 (47)	6 (32)				
Postoperative dry mouth	15 (79)	15 (79)	3 (16)	8 (42)	2 (11)	5 (26)
Visual disturbance	7 (37)	4 (21)	0 (0)	8 (42)	0 (0)	2 (11)

The incidence of the various degrees of nausea and vomiting for the three time periods is shown in Table 2. It can be seen that severe nausea or vomiting occurred in all patients who received placebo, and 13 patients (68%) who received transdermal hyoscine. There was no statistical difference in the number of doses of metoclopramide which the two groups received on any day postoperatively. In addition, there was no significant difference in the number of doses of papaveretum that each group were given on the 3 days following surgery, and no correlation between the papaveretum dosage and nausea/vomiting score.

The incidence of dry mouth and visual disturbances, at different periods, are shown in Table

3. The only difference of statistical significance occurred on the second day, when eight patients in the hyoscine group complained of disturbed vision; no patient who had received placebo did so ($p < 0.004$). One patient complained of skin irritation after 48 hours, but that was due to the overlying Band-aid.

Discussion

Hyoscine, given intramuscularly, has been shown to be an efficient pre- and postoperative anti-emetic when nausea and vomiting was induced by morphine,[6] but its action does not last as long as morphine. Hyoscine is the most effective treatment for motion sickness, especially in combination with dexamphetamine,[7] but its action is short-lived. It probably acts via muscarinic cholinergic receptors which occur at inputs to the vomiting centre, particularly from the vestibular centre and the gastrointestinal tract.[8]

There are many known factors that influence both the incidence and severity of postoperative nausea and vomiting.[1,9,10] These include age, sex, weight, previous postoperative sickness, susceptibility to motion sickness, type of anaesthesia and surgery, and degree of postoperative pain. In this study, we attempted to eliminate the effects of as many of these factors as possible by using matched pairs of patients. The two groups were also comparable for age, weight, and analgesia. No correlation was found between nausea and vomiting scores and weight.

This study has demonstrated a significant reduction in nausea and vomiting in those patients given transdermal hyoscine, using the simple nausea/vomiting score, and no increase in side effects for the first 24 hours postoperatively. The number of doses of anti-emetic given, however, showed no such difference. The probable reason for this is that six patients who actually vomited were not given any anti-emetics: it is possible that they refused these drugs when offered, for whatever reason (e.g. dislike of injections). Alternatively, the nurses, who were understaffed and had to cope with many patients, were not able to offer anti-emetics at the time they were needed.

The anti-emetic effect of transdermal hyoscine did not persist beyond 24 hours. The incidence of nausea and vomiting in both groups had markedly decreased after the first 24 hours and was so low on the third day that no difference in the two groups could be demonstrated. However, if it is due solely to a drug effect, the reduction in nausea and vomiting would be expected to continue into the second 24 hours. All the information[5-8] on the drug delivery system indicates that the drug is reliably absorbed at a fairly constant rate for 72 hours, so its lack of effect is probably not due to deficiencies in drug delivery. Since tolerance to the antimotion sickness effects of transdermal hyoscine at 72 hours compared to 12 hours has been reported,[11] it is possible that tolerance to the anti-emetic effects had developed.

Of the two side effects observed, the incidence of dry mouth was not different between the groups for any of the time periods studied. Presumably, any dryness noted from the hyoscine would be masked by pre- and postoperative oral fluid restriction. Similarly, disturbance of vision in the first 24 hours may be masked by the residual effects of the anaesthetic and muscle relaxants. However, there is a very significant difference in the amount of visual disturbance in the 48-hour period, with more in the group using hyoscine. This did not persist beyond 48 hours. Since by this time there was no decrease in the incidence of nausea and vomiting in the transdermal hyoscine group, there would seem little point in persisting with this therapy after the first 24-hour period postoperatively. Other reported side effects of transdermal hyoscine, such as confusion, restlessness, sedation[12] or urinary retention were not specifically recorded in this pilot study.

Although transdermal hyoscine reduced postoperative nausea and vomiting, the incidence of severe nausea and vomiting in the treatment group in the first 24 hours was 68%, a figure still unacceptably high. The preparation alone is unlikely to be the answer for this distressing, if usually minor, side effect of anaesthesia and surgery. It may be that transdermal hyoscine will find its place as part of a polypharmacological approach, using combinations of drugs which act differently on the vomiting reflex.

Acknowledgments

We wish to thank the consultant gynaecologists at the Churchill Hospital, Oxford, for their help in this study of their patients. We are grateful to our colleagues in the Nuffield Department of Anaesthetics and the ward nursing staff for their ready help and cooperation.

References

1. Palazzo MGA, Strunin L. Anaesthesia and emesis. I: etiology. *Canadian Anaesthetists' Society Journal* 1984; **31:** 178–87.
2. McCauley ME, Royal JW, Shaw JE, Schmitt LG. Effect of transdermally administered scopolamine in preventing motion sickness. *Aviation, Space and Environmental Medicine* 1979; **50:** 1108–11.
3. Price NM, Schmitt LG, McGuire J, Shaw JE, Trobough G. Transdermal scopolamine in the prevention of motion sickness at sea. *Clinical Pharmacology and Therapeutics* 1981; **29:** 414–9.
4. Shaw JE, Urquhart J. Transdermal drug administration–a nuisance becomes an opportunity. *British Medical Journal* 1981; **283:** 875–6.
5. Chandrasekaran SK, Michaels AS, Campbell PS, Shaw JE. Scopolamine permeation through human skin *in vitro*. *American Institute of Chemical Engineers Journal* 1976; **22:** 828–32.
6. Clarke RSJ, Dundee JW, Love WJ. Studies of drugs given before anaesthesia. VIII. Morphine 10 mg alone and with atropine or hyoscine. *British Journal of Anaesthesia* 1965; **37:** 772–7.
7. Wood CD. Antimotion sickness and antiemetic drugs. *Drugs* 1979; **17:** 471–9.
8. Palazzo MGA, Strunin L. Anaesthesia and emesis. II: prevention and management. *Canadian Anaesthetists' Society Journal* 1984; **31:** 407–15.
9. Bellville JW, Bross IDJ, Howland WS. Postoperative nausea and vomiting IV: factors related to postoperative nausea and vomiting. *Anesthesiology* 1960; **21:** 186–93.
10. Riding JE. The prevention of postoperative vomiting. *British Journal of Anaesthesia* 1963; **35:** 180–8.
11. Greybiel A, Cranmer DB, Wood CD. Antimotion-sickness efficacy of Scopolamine 12 and 72 hours after transdermal administration. *Aviation, Space and Environmental Medicine* 1982; **53:** 770–2.
12. Johnson P, Hansen D, Matarazzo D, Petterson L, Swisher C, Trappolini A. Transderm Scop Patches for prevention of motion sickness. *The New England Journal of Medicine* 1984; **311:** 468.

P, 24,519.

Anaesthesia, 1986, Volume 41, 21–26

Intramuscular midazolam premedication in small children

A comparison with papaveretum and hyoscine

M. B. TAYLOR, P. R. VINE AND D. J. HATCH

Summary

Midazolam 0.2 mg/kg was compared as an intramuscular premedication in small children with papaveretum and hyoscine 0.4 and 0.008 mg/kg. Midazolam produced satisfactory sedation and anxiolysis and in the early postoperative period patients were significantly more awake ($p<0.05$).

Key words

Anaesthesia; paediatric.
Premedication; narcotic, midazolam.

Midazolam is a water soluble benzodiazepine of short half-life, which has been shown to have anxiolytic, sedative, hypnotic and amnesic properties. It is well absorbed intramuscularly[1] and studies in adult patients have shown it to be a good premedicant by this route.[2–4] The purpose of this study was to assess the safety and efficacy of intramuscular midazolam in children before surgery. It was compared in a double blind trial with intramuscular papaveretum and hyoscine, which is used routinely as a premedicant at this hospital.

Methods

Fifty-nine children, aged 2–10 years and over 15 kg in weight, admitted for elective inpatient or day case surgery (general, orthopaedic or ENT) under general anaesthesia which was expected to last less than 90 minutes, were studied (Table 1).

Table 1. Demography of patients

	Midazolam + atropine	Papaveretum + hyoscine
Number of patients	29	30
Male: female	18:11	25:5
Inpatient: day	16:13	19:11
Age (mean, years)	5.61	5.59 (SED 0.555) NS
Weight (mean, kg)	22.4	21.3 (SED 1.871) NS

SED, standard error of differences.
NS, not significant.

Approval was obtained from the hospital Ethical Committee and informed consent from the parents. A preliminary, uncontrolled dose finding study established the minimum satisfactory intramuscular premedicant dose of midazolam in small children to be 0.2 mg/kg.

Each child was visited by one of the in-

M.B. Taylor*, MB, BS, FFARCS, Registrar, P.R. Vine†, BSc, MB, BS, MRCP, FFARCS, Registrar, D.J. Hatch, MB, BS, FFARCS, Consultant, Department of Anaesthesia. The Hospital for Sick Children, Great Ormond Street, London WC1.
Present appointments:
*Senior Registrar, Hammersmith Hospital, Du Cane Road, London W12 0HS..
†Senior Registrar, King's College, Hospital, Denmark Hill, London SE5.

0003–2409/86/010021 + 06 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Table 2. Emotional state of patients on entry to trial and sedation before and after premedication

Group	Anxiety on entry to trial (%)		Sedation before premedication (%)				Sedation 30 minutes after premedication (%)				Sedation before induction (%)			
	None/ mild	Moderate/ severe	Turbulent	Awake and anxious	Awake and calm	Asleep	Turbulent	Awake and anxious	Awake and calm	Asleep	Turbulent	Awake and anxious	Awake and calm	Asleep
Midazolam —atropine ($n = 28$)	8 (29)	20* (71)	1 (4)	14 (50)	13 (46)	0	0	6 (22)	20 (74)	1 (4)	2 (7)	4† (14)	22† (78)	0
Papaveretum —hyoscine ($n = 29$)	17 (59)	12 (41)	0	10 (33)	19 (66)	0	0	3 (11)	18 (64)	7 (25)	2 (7)	5 (17)	21 (72)	1 (3)

*$p < 0.05$ compared to papaveretum–hyoscine group.
†$p < 0.05$ compared to same group before premedication.

Table 3. Induction of anaesthesia

	Unsatisfactory	Satisfactory	Very good
Midazolam –atropine	6	11	11
Papaveretum –hyoscine	3	10	16

vestigators on the evening or morning before surgery for assessment and explanation. Patients were randomly allocated to receive either midazolam 0.2 mg/kg with atropine 0.02 mg/kg (maximum 0.5 mg) or papaveretum 0.4 mg/kg with 0.008 mg/kg hyoscine intramuscularly, 30–60 minutes pre-operatively. This was prescribed by the patients' House Surgeon and the investigators remained unaware of premedicant type. No child received night sedation prior to surgery. Children were assessed by one of the investigators on entry to the trial, before and after premedication, in the anaesthetic room and postoperatively for the following: degree of anxiety and sedation on a four point scale (Table 2), presence of nausea and vomiting, respiratory rate, heart rate and arterial blood pressure. The cardiorespiratory observations were measured intra-operatively at 15-minute intervals and, at the end of anaesthesia; the times taken to respond to stimulus and command were recorded. In addition, induction of anaesthesia was graded on a three point scale as unsatisfactory, satisfactory or very good. Anterograde amnesia was tested for with a picture (train, cat, flower or teddy bear, selected at random) shown to each child in the anaesthetic room and again 2 and 24 hours postoperatively.[5]

Forty-six of the children received an inhalational induction of anaesthetic with cyclopropane while the remainder received thiopentone. Maintenance was with nitrous oxide, oxygen and halothane, delivered via a T-piece or Mapleson A system. Any adverse events were recorded, as was the administration of analgesics postoperatively. The injection site of the premedication was inspected 2 and 24 hours postoperatively for any tenderness or local reaction.

The statistics used to analyse the results were analysis of variance with standard errors of difference (SED) for continuous data, or the Chi squared test with Yates' correction.

Results

The two groups of patients in this study were similar with respect to age, weight and distribution of inpatient and day cases, although there were more males than females (Table 1). The results of two patients were excluded from the trial because of breaches of the protocol.

There was a significant difference in baseline anxiety assessment between the two groups ($p < 0.05$). This is reflected in the degree of sedation prior to premedication, where twice as many papaveretum–hyoscine patients were awake and calm (66%) than awake and anxious, compared to almost equal numbers in each group for the midazolam–atropine patients (Table 2). Thirty minutes after premedication and prior to induction, the majority of patients (72% and 78%, respectively) were awake and calm, with no statistical differences between the two treatment groups. The midazolam group was significantly more sedated prior to induction than before the premedication was given ($p < 0.05$, Table 2).

Induction of anaesthesia was judged to be either satisfactory or very good in 78% of midazolam–atropine patients and 89% of the papaveretum–hyoscine group (Table 3). The difference was not statistically significant. Midazolam–atropine patients recovered significantly more quickly than papaveretum–hyoscine patients, taking a mean of 7.3 minutes to respond to stimulus compared to 10.8 minutes ($p < 0.02$). This difference was not seen in the times taken to be responsive to commands. After recovery, midazolam-atropine patients were significantly more awake than the papaveretum–hyoscine group ($p < 0.001$, Table 4). There was no significant difference between the two groups in either the distribution of method of induction of anaesthesia or the dose of thiopentone used in those children receiving it.

No nausea or vomiting occurred prior to operation. Postoperatively, there was no significant difference in incidence of nausea and vomiting, which occurred in 39% of midazolam–atropine and 57% of papaveretum–hyoscine patients. However, in the latter group, nausea and vomiting occurred twice as often over 2 hours postoperatively than before this time.

Anterograde memory loss 2 hours postoperatively was significantly greater in the patients who received midazolam–atropine (25%) than in the other group (3.0%, $p < 0.05$). This

Table 4. Recovery from anaesthesia

	Time (minutes) after end of anaesthesia when responsive to		State on recovery	
	Stimulus	Commands	Awake or crying	Drowsy or asleep
Midazolam –atropine	7.3*	15.3	19†	9
Papaveretum –hyoscine	10.79	17.7	3	26

*p<0.01.
†(number of patients) p<0.001.

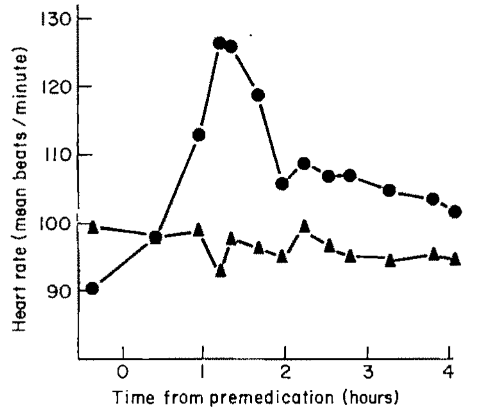


Fig. 1. Changes in heart rate following premedication and during and after surgery. (●), midazolam–atropine; (▲), papaveretum–hyoscine.

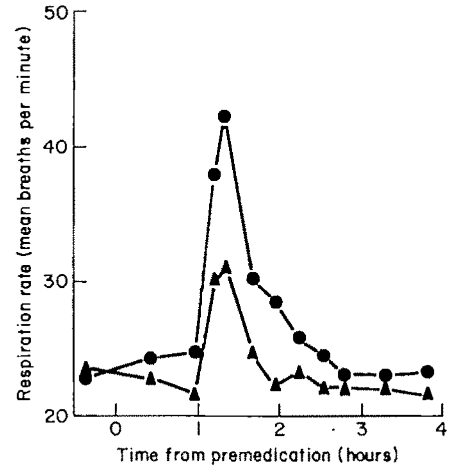


Fig. 2. Changes in respiratory rate following premedication and during and after surgery (●), midazolam–atropine; (▲), papaveretum–hyoscine.

difference was no longer apparent after 24 hours. The 24-hour result, however, depended on parental observation of the day case patients. Observation of intramuscular injection sites revealed no significant problems with either group.

Prior to surgery, there was little difference in the cardiorespiratory observations after premedication, though the respiratory rate fell in the papaveretum–hyoscine group. Peroperatively, respiratory rate and heart rate rose significantly in the midazolam–atropine patients, compared to the papaveretum–hyoscine group ($p < 0.001$, Figs 1 and 2). Papaveretum–hyoscine patients had a lower systolic blood pressure during anaesthesia, which rose on recovery, while in the other group the systolic blood pressure was higher during anaesthesia and fell on recovery. There was no overall significant difference in either systolic or diastolic pressure between the two groups.

Only seven children required parenteral analgesics in the 24 hours following operation, and six of these came from the midazolam–atropine patients. However, no significance can be drawn as operation type was not matched between the groups. There were few adverse events in either group. One 4-year-old child was confused and restless 15 minutes after receiving midazolam, but soon afterwards became sedated. Two day case patients who received papaveretum–hyoscine had sufficient postoperative vomiting to cause overnight admission.

Discussion

Many investigators have commented on the superiority of the oral route of premedication in children,[6,7] or found that no premedication at all is satisfactory.[8] At this hospital, however, the parenteral administration of a sedative together with an anticholinergic, usually papaveretum and hyoscine for children over 15 kg, is preferred. This is because experience of oral premedicants has not found them as satisfactory with regard to acceptability to the children, reliability of absorption and efficacy. This is especially the case where predictable results are essential, e.g. children undergoing multiple procedures, cardiac operations and mental handicap. This choice is partly influenced by the specific circumstances prevailing at the hospital, such as the large turnover of patients, absence of pre-induction rooms and the distances children have to travel to the operating theatres.

The dose of midazolam used in the study (0.2 mg/kg) is larger than that found effective in adults, where various intramuscular dosage and premedication studies using midazolam have found a dose of 0.07–0.1 mg/kg effective.[2-4] Doses of above 0.15 mg/kg intramuscularly in adults have produced loss of consciousness.[9]

Only one child receiving midazolam was asleep at 30 minutes and none at 60 minutes. Midazolam did not produce local irritation or reaction when given intramuscularly in children. It was effective in producing anxiolysis and sedation, for, despite the initial greater degree of anxiety in the midazolam group, there was no difference between the two groups 30 and 60 minutes after premedication. The quality of premedication was judged better in the papaveretum–hyoscine group, but this was not statistically significant.

It has been found that the majority of adult patients would prefer not to have an amnesic premedication,[10] but this may be an advantage in children. The 25% of midazolam patients showing amnesia for the picture 2 hours postoperatively is similar to studies of oral benzodiazepines in children,[5] but less than other intramuscular midazolam studies in adults.[3,4] If induction takes place 30 minutes after midazolam, when its effects are maximal,[2] a higher incidence of amnesia may be found. The short duration of action of midazolam means the timing of administration must be precise, and this may be difficult in a busy ward.

Operative cardiorespiratory depression is significantly less with midazolam compared to papaveretum and hyoscine, and this may be an advantage in some patients. The higher respiratory rate during surgery, however, is less efficient with a T-piece system, causing an increase in deadspace and fresh gas flow requirement.[11]

In conclusion, this study has shown that midazolam is a satisfactory intramuscular sedative and premedicant in children. There is a higher incidence of retrograde amnesia with midazolam–atropine medication than with papaveretum-hyoscine and a more rapid postoperative recovery, which may be useful for some day case procedures in children. Intramuscular midazolam may also be useful in the sedation of children for minor diagnostic or therapeutic procedures.

Acknowledgments

The authors would like to thank the Nursing Staff at the Hospital for Sick Children for their help with this study and Miss K. Lewis for typing the manuscript.

References

1. Ziegler WH, Thurneysen JD, Crevoisier CL, Eckert M, Amrein R, Dubuis R. Relationship between clinical effects and pharmacokinetics of midazolam on I.M. and I.V. application to volunteers 1st comm: clinical aspects. *Arzeinmittelforschung* 1981; **31:** 2206–10.
2. Vink HR, Reeves JG, Wright D. Premedication with intramuscular midazolam: a prospective randomized double-blind controlled study. *Anesthesia and Analgesia* 1982; **61:** 933–7.
3. McAteer EJ, Dixon J, Whitwam JG. Intramuscular midazolam. A comparison of midazolam with papaveretum and hyoscine for intramuscular premedication. *Anaesthesia* 1984; **39:** 1177–82.
4. Fragen RJ, Funk DI, Avram MJ, Costello C, Debruine K. Midazolam versus hydrozine as intramuscular premedicant. *Canadian Anaesthetists' Society Journal* 1983; **30,** 136–41.
5. Burtles R, Astley B. Lorazepam in children. A double-blind trial comparing lorazepam, diazepam, trimeprazine and placebo. *British Journal of Anaesthesia* 1983; **55:** 275–8.
6. Doughty AG. The evaluation of premedication in children. *Proceedings of the Royal Society of Medicine* 1959; **52:** 823–34.
7. Richardson FJ, Manford MLM. Comparison of flunitrazepam and diazepam for oral premedication in older children. *British Journal of Anaesthesia* 1979; **51:** 313–9.
8. Desjardins R, Ansara S, Charest J. Preanaesthetic medication in paediatric day-case surgery *Canadian Anaesthetists' Society Journal* 1981; **28:** 141–8.
9. Gemperle M, Kapp W. Midazolam and anaesthesia. *British Journal of Clinical Pharmacology* 1983; **16:** 187S–190S.
10. Korttilla K, Aromaa U, Tammisto T. Patients expectations and acceptance of the effects of the drugs given before anaesthesia: comparison of light and amnesic premedication. *Acta Anaesthesiologica Scandinavica* 1981; **25:** 381–6.

Anaesthesia, 1986, Volume 41, pages 27–31

Lower limb blocks for children

Lateral cutaneous and femoral nerve blocks for postoperative pain relief in paediatric practice

L. R. McNICOL

Summary

Femoral and lateral cutaneous nerve of the thigh blocks have been performed in a group of 50 children; the method has not previously been described in paediatric practice. The technique was judged to have been successful in 48 (96%) of the children. There were no early or late complications. It is concluded that these blocks are easy to perform, even in small children and infants, and that they can produce reliable postoperative analgesia for a variety of orthopaedic and plastic procedures.

Key words

Anaesthetic techniques, regional; femoral nerve, lateral cutaneous nerve of the thigh.

Femoral nerve block is a common procedure in adult practice and although its usefulness in paediatric practice has been mentioned in textbooks on local analgesia,[1] the only reference to any series of such blocks[2] is ambiguous and does not quote a success rate. Lateral cutaneous nerve of the thigh block is gaining in popularity in adult practice, but there is no reference to its use in children, in a search of the medical literature of the past 30 years.

The aim of this study was to establish if these blocks, performed together, could produce safe reliable postoperative analgesia for children undergoing procedures on the thigh and femur.

Method

Patients

The study was limited to patients who were undergoing procedures on the lower limbs in those areas innervated by the lateral cutaneous nerve of thigh and femoral nerve, and which would produce pain severe enough to warrant the use of narcotic analgesics postoperatively. The details of the patients are shown in Table 1. The first 33 patients acted as a pilot study to ascertain what problems might be encountered; consequently, they were studied more closely than the remainder.

Anaesthesia

Premedication consisted of oral droperidol and diazepam, each in a dose of 200 μg/kg, except for three patients who received intramuscular atropine, 15 μg/kg, and two patients who received oral diazepam only. In thirty-four patients anaesthesia was induced intravenously, 30 with thiopentone, two with Althesin and two with ketamine. The rest had gaseous inductions. Anaesthesia was maintained in all 50 patients with nitrous oxide, oxygen, and halothane;

L.R. McNicol, FFARCS, Consultant, Division of Anaesthesia, Royal Hospital for Sick Children, Yorkhill, Glasgow, G3 8SJ.

0003–2409/86/010027 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Details of patients in the study. Range (mean, S.D.)

Number of patients	Age (years)	Weight (kg)	Number of patients $\leqslant$ 1 year	Number of patients $\leqslant$ 10 kg	Procedures			
					D.O.	S.S.G.	Plate	Osteo.
50	0.5–14.8 (5.8, 4.7)	7–51.2 (21.3, 12.1)	3	5	34	7	6	3

D.O. = Derotation Osteotomy; S.S.G. = Split skin graft; plate = insertion or removal of pin and plate; osteo. = other osteotomies.

ventilation of the lungs was controlled in 16 cases.

No narcotic analgesic was administered at any time in the anaesthetic sequence, so that the efficacy of the blocks could be assessed. Following induction of anaesthesia, the lateral cutaneous nerve of thigh and the femoral nerve were blocked and the patients assessed for side effects due to either the local analgesic or adrenaline. None were noted.

Anatomy and blocking techniques

The lateral cutaneous nerve of the thigh is a pure sensory nerve which arises from the lumbar plexus from the segments $L_{2,3}$, and innervates the skin of the outside of the thigh (Fig. 1). It enters the thigh deep to the inguinal ligament and continues deep to the fascia lata which it eventually pierces to become subcutaneous on the outside of the thigh. It is an easy nerve to block in adults and, apart from the remote possibility of dysaesthesia or hypoaesthesia, there appear to be no other risks.

It is blocked using the standard technique described in textbooks of local anaesthesia,[3] medially to the anterior superior iliac spine and inferiorly to the inguinal ligament (Fig. 2). A 23-gauge needle with a syringe of local analgesic attached is inserted at position X, aiming from the inguinal ligament in the direction of the nerve The needle point should pass deep to the fascia lata and is moved in and out a few millimetres while injecting local analgesic in a fan shape almost parallel to the skin. The drug used was bupivacaine 0.5% with adrenaline 1:200000; the dose varied from 0.5–1.0 mg/kg. It is the author's experience that addition of adrenaline speeds up the onset of analgesia when bupivacaine is used.

The femoral nerve is also a branch of the lumbar plexus rising from the L_{2-4} segments. It is a mixed motor and sensory nerve and supplies sensation to the front and part of the inside of the thigh (Fig. 3). It is also the most important nerve supplying sensation to the periosteum of the femoral shaft and its motor component supplies the quadriceps muscles which extend the knee. It

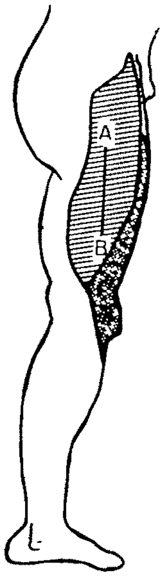


Fig. 1. Area of sensation supplied by the lateral cutaneous nerve of thigh. (▤) Combined blocks of this nerve and the femoral nerve (░) provide analgesia to a large area of thigh, of use following split skin grafts. AB, line of incision for many common paediatric orthopaedic procedures.

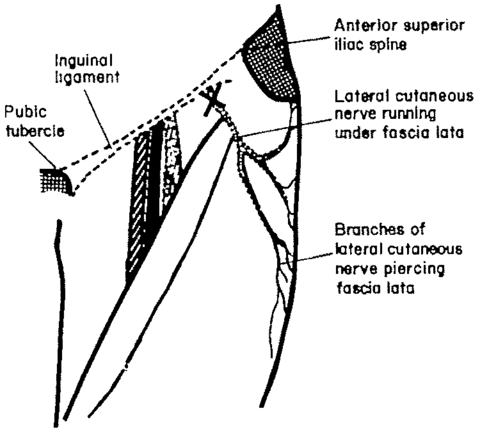

Anterior superior iliac spine
Inguinal ligament
Lateral cutaneous nerve running under fascia lata
Pubic tubercle
X
Branches of lateral cutaneous nerve piercing fascia lata

Fig. 2. Anatomy of lateral cutaneous nerve of thigh.

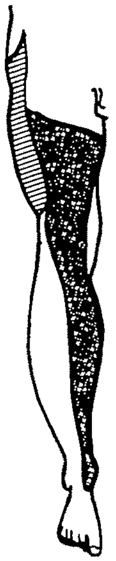


Fig. 3. (▨), area of sensation supplied by the femoral nerve. The motor component supplies power to the quadriceps muscles, spasm of which often accompanies surgery on the femur, adding to postoperative pain.

divides into several branches as it enters the leg deep to the inguinal ligament and lateral to the femoral artery, (Fig. 4) and is blocked using the standard technique described in textbooks of local analgesia.[3] The anaesthetist stands on the opposite side and palpates the femoral artery at a point where it has passed under the inguinal ligament. A 23-gauge needle, with the syringe of local analgesic attached, is inserted perpendicularly to the skin, 0.5–1.0 cm lateral to the femoral artery at point X. The local analgesic is injected with the needle point moving in a fan shaped direction, while being moved in and out a few millimetres at a time. Care should be taken to aspirate when in the vicinity of the femoral artery. Bupivacaine 0.5% with adrenaline 1:200 000 was used in a dose of 0.5–1.0 mg/kg. The early complication of haematoma is a possibility because of the proximity of the femoral blood vessels, but it should not be clinically significant. Residual nerve involvement is a remotely possible complication.

Postoperative management

Thirty-three patients (group 1) acted as a pilot study and had their pain assessed in the recovery room by the theatre nursing staff and again in the ward once time had been allowed for them to settle. The method of assessment was a 10-cm linear analogue pain scale. This group were prescribed only papaveretum 1 mg/3kg administered four-hourly on an 'on demand' basis at the discretion of the ward nursing staff. They were unaware that the patients had received any analgesia apart from the block.

The remaining 17 patients (group 2) differed in that they were prescribed oral dihydrocodeine (DF118) in a dose of 0.3–0.5 mg/kg. This was administered 6-hourly routinely until midnight on the day of operation, in an attempt to help the patients through that period when the blocks began to wear off. They were also prescribed intramuscular papaveretum 1 mg/3 kg/6-hourly 'on demand'. The nursing staff were aware that the blocks were the only form of analgesia administered to this group during the operative

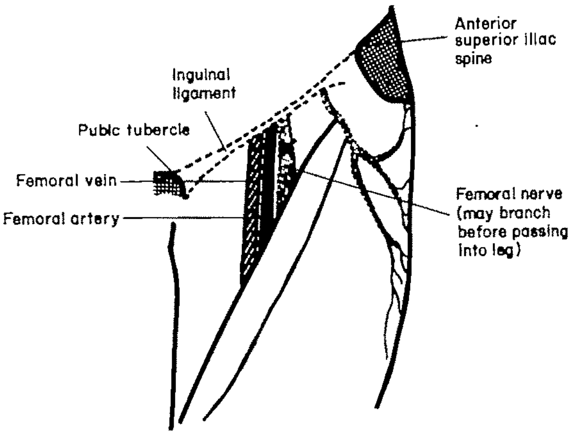

Anterior superior iliac spine
Inguinal ligament
Pubic tubercle
Femoral vein
Femoral artery
Femoral nerve (may branch before passing into leg)

Fig. 4. Anatomy of the femoral nerve.

period and they were instructed that any patient thought to be suffering from pain because of a failed or incomplete block was to have immediate intramuscular papaveretum and that the dihydrocodeine was to be withheld.

The postoperative pain scores and analgesic requirements were therefore both used to assess the efficacy of 33 blocks, while the remaining 17 were assessed purely on analgesic requirements.

Results

Group 1

The pain scores for these patients are shown in Table 2. Twenty-seven patients were assessed as having no pain in the recovery room, while six had mild pain. Nobody was thought to be suffering moderate to severe pain. After being given time to settle in the ward, 28 patients were pain free, three had mild pain and two had moderate pain. No patients were assessed as having severe pain.

Table 2. Postoperative pain scores for Group 1 ($n = 33$)

		Mild pain			Moderate pain			Severe pain			
Pain scores	0 No pain	1	2	3	4	5	6	7	8	9	10 Pain as bad as can be
Number of patients											
in recovery room	27	3	2	1	0	0	0	0	0	0	0
in ward	28	2	0	1	0	1	1	0	0	0	0

Analgesic requirements. Fourteen patients required no postoperative analgesia. The remaining 19 patients required papaveretum at 2–17 hours (mean 10.6, SD 4.5). Three patients required narcotic analgesia within 4 hours of the blocks being performed; two of these have been considered as failures and one as a qualified success. This was an 8-year-old boy who had split skin grafts taken from his thigh. He had no pain in the distribution of the blocked nerves, but only on the back of the thigh, in the area of innervation of the sciatic nerve. This was a bad choice of anaesthetic, since the surgical procedure was more extensive than initially thought. The failures were two girls of 1½ and 3 years who had derotation osteotomies. No explanation can be given for these failures except that they must have been the result of faulty technique. It is not possible to say if it was the femoral and/or the lateral cutaneous nerve block which had failed in these cases.

Group 2

Analgesic requirements. All 17 patients were assessed as having had successful blocks and were commenced on routine dihydrocodeine. Four also required intramuscular papaveretum as the blocks wore off at 9, 11, 12 and 13 hours. If the results of both groups are combined and if the boy who had the skin taken from the back of his leg is counted as a success, then the failure rate is two out of 50 patients (4.0%). No early complications such as haematoma or infection at the site of injection were present in any patients, although it must be noted that not all of them could be fully examined in the immediate postoperative period because of the presence of hip spicas. Following removal of these, patients were carefully examined for motor or sensory nerve damage. None was found in any patient.

Discussion

Some of the most painful operations in paediatric practice are performed on the lower limbs. These range from major orthopaedic procedures to the taking of split skin grafts, usually in patients suffering from burns.

The estimation of postoperative pain is always difficult, but especially so with children. In this study, reliance has been placed on the assessment of the patients' pain by the normal theatre and ward staff; of the variables assessed, the postoperative analgesic requirements and their timing were considered to be the most important. The failures were considered to be those children requiring postoperative analgesia within 4 hours of the block being performed, since with bupivacaine one would expect a period of analgesia longer than that produced by alternative methods, e.g. papaveretum.

The routine administration of dihydrocodeine was not considered to have masked any unsuccessful blocks because the nursing staff were instructed that the patient had to be awake and obviously pain free before it was administered. It remains the author's opinion that oral analgesia should be commenced as soon as possible in all patients who have had a regional nerve block to prevent the onset of severe pain when the block wears off. It should be noted that two children who had split skin grafts taken, had anaesthesia induced with intravenous ketamine and maintained with halothane in nitrous oxide and oxygen. They did not require postoperative analgesia, even after full recovery from the ketamine.

Although the sensory innervation of the femoral shaft is from the sciatic and femoral nerves, femoral nerve block on its own abolishes the pain of surgery by relieving most of the periosteal pain and also by relieving reflex spasm of the quadriceps. It is not necessary therefore to perform a sciatic nerve block as well.

The aim of this study was to establish the feasibility of femoral and lateral cutaneous nerve of the thigh blocks in paediatric practice, including small children and infants. All the blocks were easy to perform and were not time consuming. Blood was aspirated from the femoral artery on three occasions, but no haematoma developed, possibly as a result of using a narrow gauge needle. The success rate of 96% is encouraging enough to continue with comparative studies with other forms of analgesia.

Acknowledgments

I wish to thank Mr M.G.H. Smith, FRCS, Consultant Orthopaedic Surgeon for his part in assessing these patients postoperatively.

References

1. SCHULTE-STEINBERG O. Neural blockade for paediatric surgery. In: Cousins M.H., Bridenbaugh P.O., eds. *Neural blockade In clinical anaesthesia and management of pain.* Philadelphia: J.P. Lippincott. 1980.
2. A IZENBERG VL. (Techniques of regional anaesthesia of the extremities in association with nitrous oxide anaesthesia in children). *Vestnik Khirurgii* 1972; **108:** 88–92.
3. ENGLESSON S. Nerve block in the region of the hip joint. In: Eriksson. E., ed. *Illustrated handbook in local anaesthesia.* London: Lloyd-Luke. 1979.

Anaesthesia, 1986, Volume 41, pages 32–38

Longterm treatment with epidural opioids

A retrospective study comprising 150 patients treated with morphine chloride and buprenorphine

P. CARL, M. E. CRAWFORD, O. RAVLO AND V. BACH

Summary

During a 2-year period, 150 patients were treated with epidural opioids for more than 7 days; 89 received morphine and 61 buprenorphine. In 16 cases, medication was changed from morphine to buprenorphine, and in 6 from buprenorphine to morphine. In 19 patients in each group, the disease process was benign. The median daily dose of morphine was 17 mg given by an average of 2.9 injections; the corresponding figures in the buprenorphine group were 1.3 mg and 2.6 injections. The mean duration of treatment was 49 days (7–397) in the morphine group and 53 days (7–262) in the buprenorphine group. Satisfactory pain relief was achieved in 40 (45%) patients who received morphine and 41 (67%) patients given buprenorphine. Altering medication from morphine to buprenorphine improved analgesia in 32% of patients, while the reverse improved pain relief in a further 46% of the patients. Side effects were reported in 46% of patients given morphine and 20% given buprenorphine. Seventy-one patients were treated on an outpatient basis. In these cases, buprenorphine was administered for 89% of the total duration of treatment and morphine chloride for 52%.

Key words

Anaesthetic techniques, regional; epidural.
Analgesics, narcotic; morphine, buprenorphine.

The discovery of opiate receptors and their endogenous ligands, the endorphins,[1,2] soon led to the use of epidural morphine in the treatment of chronic pain.[3] Two years following the latter report, more than 200 clinical trials had been published, mainly dealing with postoperative pain, and only a few studies concerned with chronic pain.[4,7]

A number of opioids have been studied, including fentanyl,[8] pethidine,[9] methadone[10] and diamorphine,[11] but morphine chloride has been the drug of choice in most cases, due to its fairly long duration of action. However, its disadvantages include pruritus, nausea, vomiting, urinary retention and respiratory depression.[12–17] In order to eliminate these problems, other opioids have been suggested for epidural administration. One of these is buprenorphine, a derivative of thebaine and a mixed narcotic agonist/antagonist.[12] Following systemic administration, buprenorphine is about 30–40 times as potent as morphine, produces analgesia for 6–8 hours and is associated with only minor unwanted side effects.[12,18–23] Studies on tissue compatibility (e.g. cerebrospinal fluid) indicate that buprenorphine may safely be administered epidurally.[24]

P. Carl, MD, Senior Registrar, M.E. Crawford, MD, Senior Registrar, O. Ravlo, MD, Senior Registrar, V. Bach, MD, Senior Registrar, Department of Anaesthesia, Esbjerg Central Hospital, 6700 Esbjerg, Denmark.
Correspondence should be addressed to Dr P. Carl, Ericaparken 20, 2820 Gentofte, Denmark.

0003–2409/86/010032 + 07 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Its high lipid solubility and high affinity for opioid receptors suggest that it would be more useful than morphine for epidural use.[12]

This retrospective study is based on patients suffering from chronic pain and treated on a long term basis (≥7 days) with either epidural morphine or buprenorphine.

Methods

The study comprised 150 patients of whom 114 suffered from painful malignant diseases and 36 from painful benign diseases. The malignant conditions treated with either morphine chloride or buprenorphine represented lung cancer (9 and 5 cases), breast cancer (8 and 7 cases), cancer of the gastrointestinal tract (24 and 15 cases) urogenital cancer (17 and 10 cases), gynaecological cancer (7 and 6 cases) and others (4 and 3 cases). The benign group consisted of patients with ischaemia of the lower extremities (2 and 6 cases), multiple fractured ribs (4 and 1 cases), postoperative pain (11 and 10 cases), herpes zoster (1 and 1 case) and others (1 and 1 case).

Treatment was initiated at the hospital in all patients. Treatment on an outpatient basis was performed whenever possible and outpatient consultation took place in the department of anaesthetics. Epidural injections were administered by medical and non-medical personnel. Two types of epidural catheter were used (Portex or Braun) and they were usually inserted in the lumbar region.

Results

In 89 patients, morphine (as the chloride) was used in a concentration of either 0.4 or 0.8 mg/ml. The injection volume was 10 ml in 60% of cases and 15–20 ml in 40% of patients. The mean daily dose of morphine was 17 mg (4–60 mg) given as 2.9 injections (1–10). Sixty patients received extradural buprenorphine, with a mean daily dose of 1.30 mg (0.3–4.5 mg) given as 2.6 injections (1–6). The injected volume was 10 ml of a solution of 0.03 mg/ml.

In 16 cases, medication was changed from morphine to buprenorphine and in six cases from buprenorphine to morphine. On two occasions, medication was changed from buprenorphine to morphine chloride and again to buprenorphine.

Satisfactory pain relief was achieved in 41 (67%) patients treated with buprenorphine and in whom epidural buprenorphine was the sole analgesic treatment. Supplementary analgesics were administered to eight patients. Three patients received neuroleptics and/or steroids and six patients received bupivacaine (0.25–0.5%, 5–10 ml).

Analgesia was satisfactory in 40 (45%) patients who received epidural morphine as the sole method of pain relief. Additional treatment in a conventional manner was necessary with 17 patients. Eight patients received the abovementioned sedatives and 19 patients bupivacaine.

During the last visit to hospital additional treatment with droperidol epidurally was initiated in patients who were not receiving effective analgesia with epidural opioids. Its use was based on the hypothesis that dopamine receptor blocking agents at a selective spinal level would increase the efficacy of intrathecal opiates, and was given to four patients in the buprenorphine group and 13 in the morphine group. This resulted in improved pain relief in 80% of these patients.

Changing from morphine to buprenorphine, resulted in better analgesia in 32% of patients, but there was no effect in 68%. The reverse resulted in better analgesia in 46% of patients.

Table 1 shows duration of treatment with epidural opioids for all patients, expressed in days. In the morphine group, the mean duration of treatment was 49 days (7–397) and in the buprenorphine group 53 days (7–262). This table also shows the duration of treatment with both drugs after changing treatment and, in brackets, the total number of days of treatment.

Seventy-one patients were treated on an outpatient basis. Buprenorphine was used in 89% of these patients for the total duration of treatment and morphine for 52% (Table 2).

Forty-one (46%) of the patients treated with morphine complained of unwanted side effects; amongst these, 26 patients experienced 1 side effect, 13 patients 2 side effects and 2 patients 3 side effects. In the buprenorphine group, 12 (20%) patients complained of unwanted side effects: 10 patients with 1 side effect and 2 patients with 2 side effects (Table 3).

Treatment was changed from morphine to buprenorphine because of unwanted side effects in 17 (19%) patients, the reverse being the case with 1 (2%). With 12 (14%) patients' medication was altered from morphine to buprenorphine because of tachyphylaxis or low efficacy of the primary opioids and the opposite was the case with 12 (20%) (Table 4).

Table 1. Duration of treatment with epidural opioids expressed in days for all patients. In the column 'Total duration of treatment', the figures in brackets illustrate the total number of days of treatment with morphine chloride and buprenorphine

		Number of patients	Total duration of treatment (days)	Mean duration of treatment (days + range)
Morphine	B	18	403	22 (7– 54)
	M	65	3437	53 (7–397)
Buprenorphine	B	15	542	36 (8–219)
	M	28	1607	57 (14–262)
Morphine ↓ Buprenorphine	B	4	110 (140)	28 (6– 43)
	M	12	665 (1620)	55 (3–144)
Buprenorphine ↓ Morphine	B	1	5 (9)	
	M	5	318 (653)	64 (17–112)
Buprenorphine ↓ Morphine ↓ Buprenorphine	B	0	0	
	M	2	23, 47, 272 (342)	12, 24, 136 (171)

(B) Benign diseases, (M) Malignant diseases.

Table 2. Duration of treatment with epidural opioids expressed in days for patients treated as outpatients

		Number of patients	Total duration of treatment as outpatients (days)	Mean duration of treatment (days + range)
Morphine	B	1	40 (10%)	
	M	37	2019 (59%)	55 (5–346)
Buprenorphine	B	1	172 (32%)	
	M	15	975 (61%)	65 (8–250)
Morphine ↓ Buprenorphine	B	1	31 (22%)	
	M	11	1294 (80%)	118 (3–434)
Buprenorphine ↓ Morphine	B	0		
	M	3	231 (35%)	77 (8–187)
Buprenorphine ↓ Morphine ↓ Buprenorphine	B	0		
	M	2	203 (59%)	102 (24–179)

(B) Benign diseases; (M) Malignant diseases

In the morphine group, insertion of the epidural catheter, was performed in the lumbar region in 97% of cases, in the thoracic region in 2% of patients and in the cervical region in 1%. The catheter was sited in the lumbar region in all patients who received buprenorphine. In 55 of these patients, the catheter was tunnelled to the iliac region: the corresponding number in the morphine group was 76. The average number of catheter insertions in those who received buprenorphine was 1.5 per patient (1–6) and also 1.5 (1–5) in those given morphine.

Postmortem histological examination of the dura and tissue from the tunnelled subcutaneous channel was undertaken in 4 patients. Two of these received only morphine, one for 397 days with one epidural catheter. One patient had received only buprenorphine and one both drugs. No abnormalities were found in any of these patients.

The various people other than anaesthetists who injected the drugs are shown in Table 5. District nurses were involved in 76% of all injections, while the patient and/or relatives managed all medication in 24% of cases.

Table 3. Unwanted side effects of long term treatment with morphine chloride and buprenorphine.

		Morphine	Buprenorphine	Epidural + conventional analgesics
Total number of patients complaining of side effects	58/150	41/89	12/61	5/25
Nausea	16	13	3	0
Vomiting	13	10	2	1
Constipation	13	10	0	3
Urinary retention	4	4	0	0
Pruritus	2	2	0	0
Respiratory depression	0	0	0	0
Injection related pain	21	16	4	1
Dizziness	2	1	1	0
Sedation	2	1	1	0
Tachyphylaxis?	2	1	1	0

Table 4. Unwanted side effects during long term treatment eliminated by alternation between morphine chloride and buprenorphine

	Morphine	⇆	Buprenorphine	Total number of patients
Nausea	6	→	0	6
Vomiting	6	→	0	6
Constipation	2	→	0	2
Urinary retention	1	→	0	1
Pruritus	0		0	0
Injection related pain	1	→	0	1
Dizziness	1	→	0	1
Sedation	0		0	0
Tachyphylaxis?	1	⇆	1	2
No function of primary opiate	12	⇆	11	23

Table 5. People responsible for administration of epidural opioids for 72 patients treated as outpatients

	Number of outpatients	
Responsible for injections	Morphine	Buprenorphine
Patient unaided	5	5
Patient and/or relatives	6	1
Patient and/or relatives aided by district nurse or general practitioner	8	4
district nurse and/or general practitioner	4	0
District nurse	18	21
Total	41	31

Discussion

Up to 1984, there were nine publications dealing with epidural buprenorphine,[4-6,25-29] but in only three of these was the drug used for chronic pain.[4-6] In these studies only 10 of 125 patients and 12 of 105 patients were treated with buprenorphine, the remainder received morphine. Six of the studies compare morphine and buprenorphine for postoperative pain treatment.[25-30]

The main advantage of epidural opioids would seem to be the high quality of analgesia with low dose of drug. The efficiency of epidural opioids and the number of unwanted side effects during treatment may be related to the lipid solubility and receptor affinity of the drugs used and to the dose given.

The duration of action and the analgesic efficacy of buprenorphine may be explained by its high affinity to opiate receptors, which is about 50 times greater than that of morphine, and by its lipid solubility, which is about five times greater than that of morphine.[12] High lipid solubility increases both diffusion into the spinal cord and the final concentration there. It decreases diffusion from the spinal cord into the blood stream. The risk of late respiratory depression after epidural buprenorphine is therefore low, and has not been reported to date, even though buprenorphine has been administered epidurally to several thousand patients.

On the other hand, weakly lipid soluble drugs, such as morphine, will linger in the cerebrospinal fluid and be carried away from the injection site. Eventually it will reach the fourth ventricle, where it is dangerously close to vital respiratory and cardiovascular nuclei which are rich in opiate receptors.[31] Morphine reaches these vital centres slowly and so respiratory and cardiovascular depression may not occur until many hours after the drug is administered, and several observations of late respiratory depression have been described.[13] The ideal opioid for epidural use must combine high lipid solubility with strong receptor affinity, qualities that are possessed by buprenorphine.

The high lipid solubility of buprenorphine compared to morphine may also explain why the effective epidural and intravenous doses are similar, whereas the effective epidural dose of morphine is markedly lower than the systemic dose.[18] It was also our experience, during a 4-year study period, that buprenorphine 0.3 mg is equivalent to 4 mg of morphine chloride when administered epidurally.

The mean duration of treatment with morphine was 49 days (3–397), and a similar time has been reported in another study;[4] no references about buprenorphine exist.

Sixty per cent of our patients given morphine had a mean daily dose of 17 mg in three injections. Other studies report a mean daily dose of 9.3–13.6 mg.[4,7] The difference may be explained, in part, by varying criteria for initiation of treatment with epidural opioids and, therefore, difference in intensity of pain. Forty per cent of the patients who received buprenorphine had a mean daily dose of 1.3 mg given in 2.6 injections, which has also been reported in another study.[5]

Satisfactory pain relief was achieved with 67% and 45% of patients treated with buprenorphine and morphine respectively, as the sole analgesics. In other studies,[4,6] figures of 65% and 92% have been reported for morphine. From a theoretical point of view, no unwanted side effects would be expected following administration of epidural opioids, due to the site of action. However, side effects were recorded and may be regarded as a systemic action caused by absorption from epidural vein and/or a direct rostral spread produced by circulation of spinal fluid.[32] The incidence of side effects of longterm treatment is low compared to studies dealing with postoperative pain, probably due to addiction to epidural opioids during longterm treatment.[32,33] Unwanted side effects with epidural buprenorphine were much less frequent than those after epidural morphine. This paucity of side effects associated with epidural buprenorphine may also be explained by a lipid solubility so great that a very low concentration of drug in the cerebrospinal fluid reaches the brain stem, where these side effects are elicited.[34]

In 17 patients, the treatment was changed from morphine to buprenorphine because of unwanted side effects and in these cases the side effects disappeared. Only in 1 case was the treatment changed from buprenorphine to morphine chloride because of side effects. Again, this may be interpreted by the physicochemical properties of the agents, a hypothesis confirmed by Zenz *et al.*[30]

The morphine was prepared in ampoules ready for use, but buprenorphine had to be diluted with normal saline before injection. This slightly more difficult procedure with buprenorphine did not cause problems for the patients or the district nurses. Outpatients, relatives and district nurses were all carefully instructed on the theory and use of epidural opioids before treatment was started and all were ordered to contact the responsible department of anaesthesia whenever alteration of frequency or volume of injection was presumed necessary. Due to restricted duty hours (0800 until 1800) for district nurses in Denmark, only two daily consultations were available, thus forcing patients and their relatives to take part in medication procedures.

In conclusion, both morphine and buprenorphine are suitable for long term treatment when given epidurally, but buprenorphine is preferable for many cases, due to the lower incidence of side effects.

References

1. Hughes J. Isolation of an endogenous compound from the brain with pharmacological properties similar to morphine. *Brain Research* 1975; **88:** 295–308.
2. Pert CB, Snyder SH. Opiate receptor: demonstration in nervous tissue. *Science* 1973; **179:** 1011–4.
3. Behar M, Olshwang D, Magora F, Davidson T. Epidural morphine in treatment of pain. *Lancet* 1979; **1:** 527–8.
4. Andersen HB, Benveniste D, Bitch-Larsen L, Carl P, Crawford M, Djernes M, Eriksen J, Grell AM, Henriksen H, Jansen E, Kaalund-Jørgensen HO, Laugesen L, Lønholdt C, Neumann P, Pedersen JEP, Wolff J. Long-term treatment with extradural opiates. *Ugeskrift for Laeger* 1982; **136:** 2633–7.
5. Crawford ME, Andersen HB, Augustenborg G, Bay J, Beck O, Benveniste D, Carl P, Djernes M, Eriksen J, Grell AM, Henriksen H, Johansen SH, Kaalund-Jørgensen HO, Møller IW, Pedersen JEP, Ravlo O. Pain treatment on outpatient basis utilizing extradural opiates. A Danish multicentre study comprising 105 patients. *Pain* 1983; **16:** 41–7.
6. Zenz M, Piepenbrock S, Schappler-Scheele B, Hüsch M. Epidural morphine analgesia. (PMA) III. Cancer pain. *Anaesthesist* 1981; **30:** 508–13.
7. Zenz M, Schappler-Scheele B, Neuhaus R, Piepenbrock S, Hilfrich J. Long-term peridural morphine analgesia in cancer pain. *Lancet* 1981; **1:** 91.
8. Wolfe MJ, Davies GK. Analgesic action of extradural fentanyl. *British Journal of Anaesthesia* 1980; **52:** 357–8.
9. Cousins MJ, Mather LE, Glynn CJ, Wilson PR, Graham JR. Selective spinal analgesia. *Lancet* 1979; **1:** 1141–2.
10. Bromage PR, Camporesi E, Chestnut P. Epidural narcotics for postoperative analgesia. *Anesthesia and Analgesia* 1980; **59:** 473–80.
11. Houlton PG, Reynolds F. Epidural diamorphine and fentanyl for postoperative pain. *Anaesthesia* 1981; **36:** 1144–5.
12. DeCastro J, Lecron L. Peridurale Opiatanalgesie. Verschiedene Opiate. Komplikationen und nebenwirkungen. In: Zenz M, ed. *Peridurale Opiatanalgesie.* Stuttgart, New York: Fischer, 1981: 103–28.
13. Gustafsson LL, Schildt B, Jacobsen K. Adverse effects of extradural and intrathecal opiates: report of a nationwide survey in Sweden. *British Journal of Anaesthesia* 1982; **54:** 479–86.
14. Lanz E, Theiss D, Riess W, Sommer U. Epidural morphine for postoperative analgesia: a double-blind study. *Anesthesia and Analgesia* 1982; **61:** 236–40.
15. Müller H, Börner U, Stoyanov M, Hempelmann G. Perioperative Analgesie durch peridurale Opiatgabe. In: Hempelmann G, Müller H, eds. *Peridurale Opiat-analgesie.* Bibliomedizine: Melsungen, 1981: 103–28.
16. Yaksh TL, Müller H, eds. Spinal opiate analgesia. Experimental and clinical studies. *Anaesthesiology and Intensive Care Medicine.* 1982; **144:** 47–113.
17. Zenz M, Piepenbrock S, Otten B, Otten G, Neuhaus P. Epidural morphine analgesia. Postoperative period. *Anaesthesist* 1981; **30:** 77–82.
18. Downing JW, Leary WP, White ES. Buprenorphine: a new potent long-acting synthetic analgesic. Comparison with morphine. *British Journal of Anaesthesia* 1977; **49:** 251–4.
19. Harcus AH, Ward AE, Smith DW. Buprenorphine in postoperative pain: results in 7500 patients. *Anaesthesia* 1980; **35:** 382–6.
20. Kamel MM, Geddes IC. A comparison of buprenorphine and pethidine for immediate postoperative pain relief by the i.v. route. *British Journal of Anaesthesia* 1978; **50:** 599–603.
21. Kay B. A double-blind comparison of morphine and buprenorphine in the prevention of pain after operation. *British Journal of Anaesthesia* 1978; **50:** 605–9.
22. Ravjover I, Alon E, Hossli G. Buprenorphin und Nicomorphin im klinischen doppelblind Versuch zur postoperativen Schmerzbekämpfung. *Anäthesie und Intensiv Notfallmedizine* 1981; **16:** 340–2.
23. Tigerstedt I, Tammisto T. Double-blind, multiple-dose comparison of buprenorphine and morphine in postoperative pain. *Acta Anaesthesiologica Scandinavica* 1980; **24:** 462–8.
24. Börner U, Müller H, Stoyanov M, Hempelmann G. Epidurale Opiat-analgesie. Gewebe-und Liquorverträglichkeit der opiate. *Anaesthesist* 1980; **29:** 570–1.
25. Cahill J, Murphy D, O'Brien D, Mulhall J, Fitzpatrick G. Epidural buprenorphine for pain relief after major abdominal surgery. *Anaesthesia* 1983; **38:** 760–4.
26 Lanz E, Simko G, Theiss D, Glocke MH. Epidural buprenorphine—a double-blind study of postoperative analgesia and side effects. Anaesthesia and Analgesia 1984; **63:** 593–8.
27. Lecron L, Levy D, Toppet-Balatoni E. Utilization de la bupré-norphine combinée à l'étidocaine en injection péridurale. *7th World Congress of Anaesthesiologists.* Hamburg 1980: section 6: 104–20.
28. Louis C, Freye E, Hartung E, Haag W. Buprenorphin in der periduralen Leitungsanästhesie. *Anästhesie und Intensiv Notfallmedizine* 1981; **17:** 341–4.
29. Rondomanska M, DeCastro J, Lecron L. The use of epidural buprenorphine for the treatment of postoperative pain. In: Yaksh TL, Müller H, eds. Spinal opiate analgesia Experimental and clinical

studies. *Anaesthesiology and Intensive Care Medicine*. 1982; **144:** 91–4.

30. Zenz M, Piepenbrock S, Hübner B, Glocke M. Peridurale Analgesie mit Buprenorphin und Morphin bei postoperativen Schmerzen. *Anästhesie und Intensiv Notfallmedizine* 1981; **16:** 333–9.
31. Pert CB, Kuhar MJ, Snyder SH. Opiate receptor: autoradiographic localization in rat brain. *Proceedings of the National Academy of Sciences of the United States of America* 1976; **73:** 3729–33.
32. Glynn CJ, Mather LE, Cousins MJ, Wilson PR, Graham JR. Spinal narcotics and respiratory depression. *Lancet* 1979; **2:** 356–7.
33. Reiz S, Westberg M. Side-effects of epidural morphine. *Lancet* 1980; **2:** 203–4.
34. Bromage PR, Camporesi EM, Durant PAC, Nielsen CH. Rostral spread of epidural morphine. *Anesthesiology* 1982; **56:** 431–6.

Anaesthesia, 1986, Volume 41, 39–41

Computerised tomography guided lumbar sympathectomy

D. R. O. REDMAN, P. N. ROBINSON AND M. A. AL-KUTOUBI

Summary

Fifteen patients had lumbar sympathetic block using needle localisation by computerised tomography. The technique has the advantage that the needle route to the sympathetic plexus can be accurately planned, avoiding damage to other organs. In this study, 13 patients out of 15 had significant benefit from the procedure.

Key words

Anaesthetic techniques, regional; lumbar sympathetic block.

The management of peripheral vascular disease involving the lower limbs of elderly patients is a continuing challenge to all forms of treatment. Many patients still require amputation, despite the chronic natural history of the condition, the availability of direct vascular surgery and the widespread use of peripheral vasodilators.[1]

Lumbar sympathectomy may be performed surgically, but this has a reported mortality rate of up to 7 per cent, mainly due to postoperative pneumonia.[2] In an effort to decrease this mortality, chemical lumbar sympathectomy has been advocated.[3] This is normally performed with the aid of an image intensifier, but can lead to complications including first lumbar nerve neuralgia (motor loss in the hip joint and sensory loss over the first lumbar nerve dermatone), subarachnoid injection, perforation of the aorta (especially of an undiagnosed aneurysm), inferior vena cava, bowel,[3] lower pole of the kidney, or ureter,[4] and injection into the psoas muscle with a twenty per cent incidence of genitofemoral dysaesthesia.[5]

In an effort to minimise these complications, a technique was devised using computerised tomography (CT) to aid accurate placement of the needle tip prior to injection of a neurolytic agent. CT has already proved to be an effective imaging technique for siting needles for biopsy,[6,7] aspiration of abscess[8,9] and for coeliac plexus block.[6,10]

Methods

Eleven male and four female patients underwent lumbar sympathetic blockade using CT guidance. Fourteen patients were treated for peripheral vascular disease (aged 64–96) and one patient, aged 18 years, presented with hyperhydrosis. The patients were referred from geriatricians and vascular surgeons. No one was refused treatment

---

D.R.O. Redman, MB, BS, FFARCS, Senior Registrar, P.N. Robinson, MB, ChB, FFARCS, Senior Registrar, M.A. Al-Kutoubi, MD, FRCR, DMRD, Consultant, Departments of Anaesthesia and Radiology, St Mary's Hospital, Praed Street, London W2.

0003–2409/86/010039 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

because of poor physical condition and all were treated as day cases.

The scanner used was a Siemens Somatom 2 with a scan time of 5 seconds and a slice thickness of 8 millimetres. Eight millimetre table movement was used.

Technique

The patient is fasted overnight and pre-operative medication of papaveretum 10–20 mg and perphenazine 2.5 mg is administered intramuscularly one hour before the commencement of the procedure. Intravenous access is established and fentanyl 100–200 μg and diazepam 10–20 mg given incrementally until adequate sedation is achieved.

The patient is placed prone upon the scanning table with the arms outstretched above the head. The levels of the lumbar vertebrae 2, 3 and 4 are localised using the scanogram facility of the CT scanner. CT slices are taken at these levels to enable a suitable route to be planned, avoiding the transverse processes, lower pole of the kidney, bowel, aorta and inferior vena cava. If clear access to the anterolateral aspect of the vertebral body is not evident a series of slices through the vertebral body is taken at 8-mm intervals until the optimal route is found. Modern scanners have a measurement facility, which allows the distance between the proposed skin entry site and the point of injection to be measured and marked on the patient. The angle of approach can also be measured directly on the viewing monitor.

A full sterile technique is employed and the skin and paravertebral muscles are infiltrated with 1 per cent lignocaine. A 16-gauge, 16-cm needle is introduced at the selected points of entry, at the appropriate angles, to the previously measured depths (Fig. 1). Saline is injected during the introduction of the needle; loss of resistance to injection is often felt when the correct tissue plane is reached. Aspiration is performed to check that each needle is not in a vessel. The needles are repositioned if necessary and 1 ml of contrast medium (e.g. half strength solution of meglumine iothalamate 60% w/v—Conray 280) is injected at each level. Repeat CT slices are taken to show the distribution of the contrast medium. If these are satisfactory, 3 ml of 7 per cent aqueous phenol are injected at each level. The needles are now withdrawn, having first been cleared of phenol by flushing with a small amount of saline. The patient is nursed in the supine position for 4 hours and the pulse, blood pressure and respiration monitored.

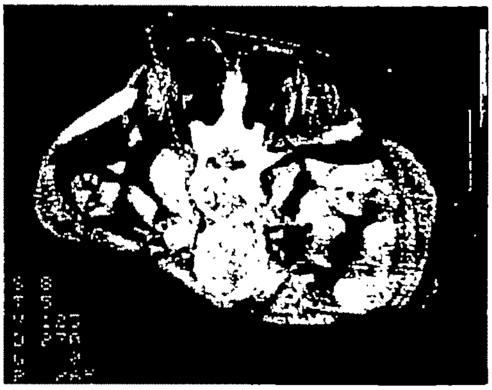


Fig. 1. Computerised tomography (CT) slice at the level of the third lumbar vertebra. The broken line shows the early point on the skin, the depth and angle of penetration required. Note the aortic aneurysm.

Results

The 15 patients were followed up, with respect to their original symptoms, over a 6-month period. Twelve of the 14 patients with ischaemic leg pain were asymptomatic and were satisfied with the degree of improvement that the block had provided. Two patients had below knee amputations performed for gangrene of the foot. The patient with hyperhidrosis was asymptomatic over the follow-up period.

Complications

Over the operative period there was one complication and this was of a minor nature; blood was aspirated from one needle after placement and this was considered to be from puncture of a lumbar vein. Resiting of the needle was successful and no change in pulse or blood pressure ensued. Two unforseen potential complications were avoided; one patient had a 7 cm undiagnosed aortic aneurysm (Fig. 1) and another a renal cyst. Neither of these structures was perforated following precise needle placement.

Discussion

The complications during the procedure of chemical lumbar sympathectomy are minimised using X ray control.[11] We suggest that CT scanning is a further refinement, since most vital structures are easily defined on the CT scan, with the possible exception of the ureter. This enables a path to be traced, avoiding abdominal organs such as the kidneys, aorta and inferior vena cava. Puncture of a lumbar vein is considered to be of no consequence.[1]

In our study, an undiagnosed abdominal aortic aneurysm and a renal cyst were discovered and we were able to take care to avoid perforation of these organs. It would therefore seem to be a better method for patients with known abdominal aneurysms or other undiagnosed pathology that could interfere with the technique of chemical lumbar sympathectomy. This includes patients with abnormal spinal anatomy, in whom chemical lumbar sympathectomy using an image intensifier is often difficult.

Accurate needle placement is readily demonstrable using CT and can easily be taught to those unfamiliar with chemical lumbar sympathectomy. The main disadvantage of this technique is the limited availability of CT scanning facilities.

Acknowledgments

The authors gratefully acknowledge the help received from the following: Dr J. Filshie, Consultant Anaesthetist, Royal Marsden Hospital, Sutton, Surrey; Miss Gillian Greenhalgh, Senior Radiographer, St Mary's Hospital, London W2; Miss Lynne Wilcox, Medical Secretary, Royal Marsden Hospital, Sutton, Surrey.

References

1. Harris PL, Read F, Eardley A, Charlesworth D. Wakefield J, Sellwood RA. The fate of elderly amputees. *British Journal of Surgery* 1974; **61:** 665–8.
2. Koikkalainen K, Luosto R, Jokinen T. Lumbar sympathectomy in the treatment of severe lower limb ischaemia in old people. *Annales Chirurgiae et Gynaecologiae* 1980; **69:** 92–6.
3. Cousins MJ, Reeve TS, Glynn CJ, Walsh JA, Cherry DA. Neurolytic lumbar sympathetic blockade: duration of denervation and relief of rest pain. *Anaesthesia and Intensive Care* 1979; **7:** 121–35.
4. Ryttov N, Boe S, Nielsen H, Jacobsen J. Necrosis of the ureter as a complication to chemical lumbar sympathectomy. Report of a case. *Acta Chirurgica Scandinavica* 1981; **147:** 78–80.
5. Scott DB, Littlewood DG. Chemical lumbar sympathectomy with radiological assessment. *Annals of the Royal College of Surgeons of England* 1982; **64:** 135.
6. Filshie J, Golding S, Robbie DS, Husband JE. Unilateral computerised tomography guided coeliac plexus block: a technique for pain relief. *Anaesthesia* 1983; **38:** 498–503.
7. Mueller PR, Wittenberg J, Ferrucci JT. Fine needle aspiration biopsy of abdominal masses. *Seminars in Roentgenology* 1981; **16:** 52–61.
8. Haaga JR, Reich NE, Havrilla TR, Alfidi RJ. Interventional CT scanning. *Radiologic Clinics of North America* 1977; **XV:** 449–56.
9. Gerzof SG, Robbins AH, Birkett DH. Computer tomography in the diagnosis and management of abdominal abscesses. *Gastrointestinal Radiology* 1978; **3:** 287–94.
10. Buy J-N, Moss AA, Singler RC. CT guided celiac plexus and splanchnic nerve neurolysis. *Journal of Computer Assisted Tomography* 1982; **6:** 315–9.
11. Hatangdi VS, Boas RA. Lumbar sympathectomy: a single needle technique. *British Journal of Anaesthesia* 1985; **57:** 285–9.

Anaesthesia, 1986, Volume 41, pages 42–45

HISTORICAL

Alfred Kirstein

Pioneer of direct laryngoscopy

N. P. HIRSCH, G. B. SMITH AND P. O. HIRSCH

Autoscopy is, therefore, a difficult morsel; until it is thoroughly absorbed into the life-blood of laryngology it will cause many a digestive disturbance.

(Kirstein, 1896)

Key words

History; Kirstein, Alfred.
Larynx; laryngoscopy.

On April 23rd 1895, in Berlin, Alfred Kirstein performed the first direct examination of the interior of the larynx. Until then laryngologists had been content with the technique of indirect laryngoscopy using mirrors, a method popularised by Garcia, Turck and Czermak.[1] Indeed, before Kirstein's discovery, it was felt that a direct view of the larynx was impossible due to the geometric relationship between the mouth and the vocal cords. However, Kirstein had learnt from his colleague Rosenheim that a scope intended to be passed into the oesophagus had accidentally slipped into the trachea and, much to the surgeon's surprise, a perfect view of the bronchial bifurcation was obtained. Armed with this knowledge, Kirstein worked furiously to devise a method of direct laryngoscopy and, in doing so, not only invented the first laryngoscope, but also laid down those principles of laryngoscopy which are still used in clinical practice throughout the world today.

Alfred Kirstein was born on the 25th of June 1863, the son of a Berlin physician. Having graduated from high school in 1882, he studied medicine at Freiberg and Strasbourg. His clinical training took place in Berlin where, in 1886, he was awarded a doctorate for his thesis entitled 'Concerning the part played by tuberculosis in the aetiology of chronic septic infections of the urinary tract.' Following short periods spent in Jena and Cologne, he returned to Berlin to work at the Institute for Legal Medicine, where he published an important work concerning 'The Diffusion of Poisons from the Corpse.'[2]

It was during 1895 that Kirstein became interested in obtaining a direct view of the larynx. Following Rosenheim's revelation, Kirstein set about devising a reproducible method of viewing the larynx directly. His initial technique involved placing an oesophagoscope into the oesophagus, and then, following topical cocaine, passing a similar but shorter (25 cm) instrument into the larynx. Using the upper incisors as a fulcrum, he obtained a view of the larynx by firmly displacing the root of the tongue and elevating the epiglottis in an anterior direction.

The question of illumination was a problem. Traditional methods of indirect laryngoscopy

---

N.P. Hirsch, MB, BS, FFARCS, Instructor, G.B. Smith, BM, FFARCS, Instructor, Department of Anesthesiology, Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06510, U.S.A., P.O. Hirsch, MB, BS, MRCGP, General Practitioner, 26 Cranes Park, Surbiton, Surrey, U.K.

0003-2409/86/010042 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

had utilised a head mirror and an incandescent light source. Kirstein found this to be inadequate for direct examination, but resolved the problem by employing electrical methods of illumination. Initially, he modified the head mirror and invented the 'forehead lamp for reflected light'. Electric rays from a lamp on the head were collected by a convex mirror and deflected at a right angle by a small perforated mirror, through which the observer was able to view the subject. He found this method of illumination satisfactory, but he used an electric light source in a second and very different way and one that is of great importance to the anaesthetist. He employed an electric hand lamp termed the 'electroscope', which had been devised by Caspar for examination of the urethra. The light rays from this lamp were collected by a lens and deflected through 90 degrees by a prism. This hand lamp was used as a handle to which the 25-cm oesophagoscope was attached (Fig. 1). He named the combination of the electroscope and the oesophagoscope 'The autoscope' and direct examination of the larynx he termed 'Autoscopy'.[3] Twenty-three days after his first view of the larynx, Kirstein gave a comprehensive demonstration of autoscopy to the Berlin Medical Association. News of his invention was also reported in the *Lancet*.[4] At this point he had already abandoned the need for the initial oesophagoscopy.

Despite the infancy of autoscopy and the autoscope, Kirstein already recognised the potential of his new discovery. In his publication *Autoskopie des Larynx und der Trachea*, he reported that 'the removal of foreign bodies from the trachea must be easier through an autoscope than by means of a tracheostomy; furthermore, catheterisation of the bronchi should now present no great difficulties'. However, it was left to Killian, the 'father of bronchoscopy' and a student of Kirstein's, to realise both these aims.[6]

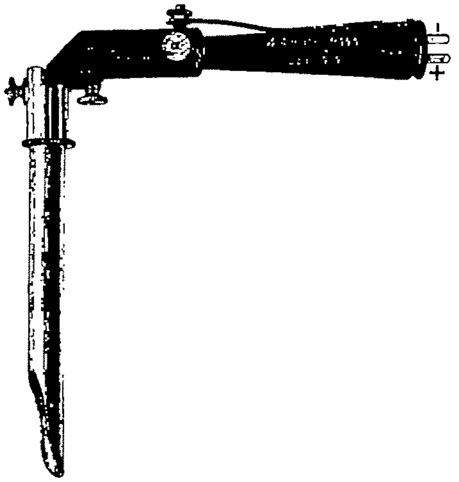


Fig. 1. Kirstein's original autoscope, consisting of an oesophagoscope and electroscope (Yale Medical Library).

Despite success with autoscopy, Kirstein was aware of a number of problems associated with the method. He was concerned about the pressure exerted by the autoscope on the upper incisors and also the need for marked extension of the neck. Furthermore, he considered cocaine to be 'poisonous'. He therefore directed his attention to overcoming these disadvantages and one month after his demonstration in Berlin, he presented a report of a modified autoscope.[7] The handle of the instrument remained the same, but in place of the oesophagoscope was attached one of two different designs of blade (Fig. 2). The standard blade, seen attached to the handle in the illustration, was designed to elevate the epiglottis by anterior pressure on the vallecula. The tip of the blade was thickened and well rounded in order to avoid injury to the mucous membranes. The intralaryngeal blade, shown without its handle in Fig. 2, was introduced beneath the laryngeal surface of the epiglottis. Forward and upward movement of the blade elevated the epiglottis, revealing the larynx. The similarity between these two

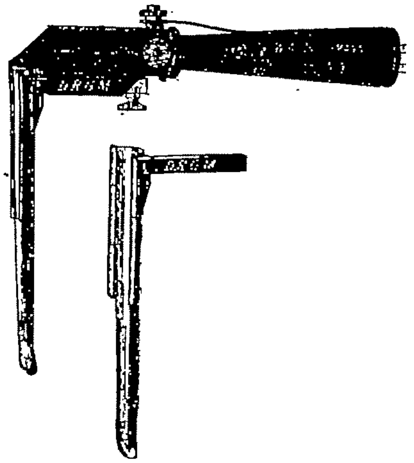


Fig. 2. Kirstein's modified autoscope. The standard blade is shown attached to the handle with the intralaryngeal blade shown below (Yale Medical Library).

blades and those described in the 1940s by Macintosh[8] and Miller[9] is remarkable.

With the introduction of his new autoscope, Kirstein found that he had overcome those problems which had concerned him. Pressure on the upper incisors could easily be avoided and, in many cases, prior use of topical cocaine was unnecessary, especially when the standard blade was used. Furthermore, he now found that extreme extension of the neck was not required for the procedure. He reported that 'the body must be placed in such a position that an imaginary continuation of the laryngotracheal tube would fall within the opening of the mouth ... When the military position is assumed, the continuation of the windpipe would strike somewhere in the neighbourhood of the root of the nose; when the head is bent comfortably backward, as in looking aloft, it would about strike the chin ... the position adopted for autoscopy must therefore be somewhere between the two positions just mentioned' (Fig. 3). Therefore, Kirstein fully appreciated the importance of rotation at the atlanto-occipital articulation and was almost certainly the first to describe what is now termed the 'sniffing the morning air' position for intubation.

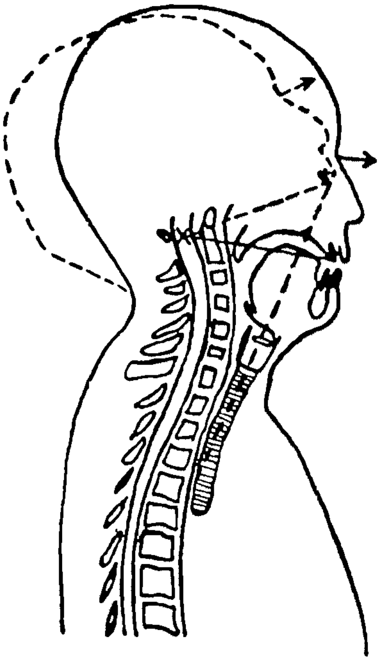


Fig. 3. Kirstein's suggested position for autoscopy (dotted lines). The solid outline shows the military position. The arrows demonstrate the visual axis (Yale Medical Library).

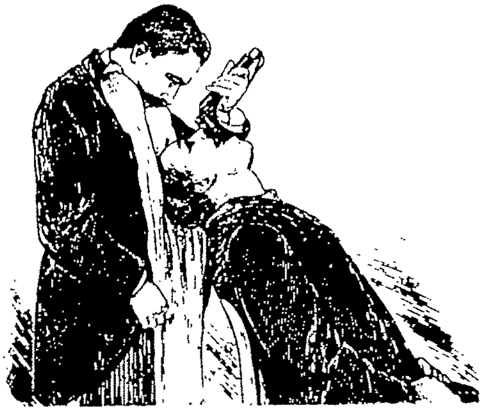


Fig. 4. Kirstein performing direct laryngoscopy. Note both the position of the patient's head and also the use of the left hand to hold the autoscope (Yale Medical Library).

The position adopted for intubation is shown in Fig. 4. With his improved autoscope, Kirstein felt that no further improvements were necessary.

On the death of his father in 1896, he succeeded to the family practice. In 1903, something unusual occurred, in that Kirstein, then aged 40 years, gave up medicine completely. Until that time, he had painted and drawn in his spare time and had always had a leaning towards artistic photography, but now he took up painting in earnest. He studied art under the Dutch painter Paul Barum in Sluis and later lived for many years in Paris, where he associated with numerous famous artists and where his own pictures were exhibited. He proved to be an excellent art historian and published a well received critique of Raphael's 'The Resurrection of Christ'. He travelled in Europe and only returned to Berlin in 1912 to exhibit his work. At the outbreak of World War I, Kirstein volunteered as a doctor and practised in this capacity in Stargard and Stettin. Believing that it was impossible to be a successful practitioner of both art and medicine, his interests returned entirely to medicine, and he never picked up his artist's brushes again.

On December 2 1922, following about eighteen months of serious ill-health, Kirstein, aged 59 years, died in the home of his elderly mother. The importance of Kirstein's discovery cannot be overlooked and, in the words of Carl von Eicken, 'The name Kirstein will, for all time, be closely connected with the history of direct laryngoscopy and the great service which he performed in the creation of this method should never be forgotten.'[10]

Acknowledgments

The authors wish to thank Dr Ferenc Gyorgyey of the Yale Medical History Library for his considerable patience and assistance during the preparation of this article, and Ms Linda Shiffrin for her secretarial help.

References

1. Fink BR. *The human larynx—a functional study.* New York: Raven Press, 1975, pp. 9–12.
2. Strassmann F, Kirstein A. Ueber Diffusion von Giften an der Leiche. *Virchow Archives* 1894; **136:** 127–59.
3. Kirstein A. Laryngoskopia directa und tracheoskopia directa. *Allgemeine Medizinische Zentralzeitung* 1895; **34:** 110–2.
4. Kirstein A. Direct laryngoscopy. *Lancet* 1895; **1:** 1132.
5. Kirstein A. Autoskopie des Larynx und der Trachea. (Laryngoskopia directa, Euthyskopie, Besichtigung ohne Spiegel). *Archiv für Laryngologie und Rhinologie* 1895; **3:** 156–64.
6. Zollner F. Gustav Killian, father of monoscopy. *Archives of Otolaryngology* 1965; **82:** 656–9.
7. Kirstein A. Fortschritte in der Untersuchung des Rachensund des Kehlkopfes ohne Spiegel. *Allgemeine Medizinische Zentralzeitung* 1895; **48:** 224–6.
8. Macintosh RR. A new laryngoscope. *Lancet* 1943; **1:** 205.
9. Miller RA. A new laryngoscope. *Anesthesiology* 1941; **2:** 317–20.
10. Von Eicken C. In memoriam Alfred Kirstein. *Zeitschrift für Hals-Nasen- und Ohrenheilkunde* 1923; **4:** 275–83.

Anaesthesia, 1986, Volume 41, pages 46–52

HISTORICAL

Stanley Rowbotham

Twentieth century pioneer anaesthetist

H. A. CONDON AND E. GILCHRIST

Summary

Stanley Rowbotham was born in 1890 and spent the first years after qualification in 1915 with the Royal Army Medical Corps (RAMC). His career in anaesthesia began after the Armistice, when he was posted with Ivan Magill to Harold Gillies's plastic surgery unit at Sidcup. Together, they laid the foundations of tracheal anaesthesia. A versatile and inventive anaesthetist, Stanley Rowbotham later pioneered in the fields of thyroid anaesthesia, basal narcosis, local and intravenous analgesia and in the use of muscle relaxants. He also introduced cyclopropane into this country.

Key words

History; Rowbotham, Edgar Stanley.

Edgar Stanley Rowbotham was recently described by a former Dean of the Faculty of Anaesthetists as 'a very significant and largely unsung pioneer in many advances in anaesthesia'.[1] This memoir seeks to place on record his life and achievements.

His grandfather was a general practitioner in Catford, whose main source of income was derived from 'Dr Birley's Nerve Syrup', a phosphorus-containing remedy for neurasthenia.[2] The business flourished and laid the foundation of the family fortunes and on his death, enabled his elder son Edgar Joseph, Stanley Rowbotham's father, to marry and embark on parenthood whilst still a medical student at Charing Cross Hospital. He qualified in 1894.

Edgar Stanley Rowbotham was born on 8th May 1890. He clearly remembered his grandfather's manufacturing laboratory and the tanks containing sticks of phosphorus. This laboratory, in the Strand, was housed in the same building as the Lancet offices. Other special childhood memories were of helping to uncrate a De Dion Bouton, ordered at the first Paris Motor Show in 1894, and of being taken to Brussels to hear Caruso sing. He inherited his parents' great love for music. At school and at university he had a distinguished record as an athlete. In due course he followed the family tradition, becoming a medical student, first at King's College, London, and then at Charing Cross Hospital.

An active member of the Officer Training Corps (OTC), he was at Aldershot with an infantry regiment when war was declared in 1914 and was sent to France. His Commanding Officer advised him to return to England to complete his studies and this he did, obtaining the Conjoint qualification in 1915. He was then immediately

---

H.A. Condon, FFARCS, Consultant Anaesthetist, The Royal National Throat Nose and Ear Hospital, Gray's Inn Road, London WC1X 8DA, E. Gilchrist, FFARCS, Honorary Consultant Anaesthetist, Honorary Archivist, The Royal Free Hospital, Pond Street, Hampstead, London NW3 2QG.

0003-2409/86/010046 + 07 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

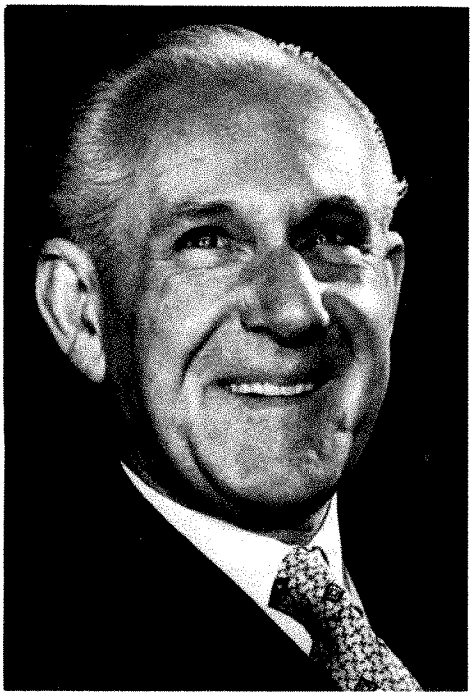


Fig. 1. Stanley Rowbotham.

commissioned in the RAMC and, because he was an able horseman, was posted to the 4th Hussars as Regimental Medical Officer. He was twice mentioned in dispatches.

In 1919 he was posted to the Queen's Hospital for Facial & Jaw Injuries at Sidcup, where a plastic surgical unit had been established under Major, later Sir Harold Gillies. Another young RAMC officer, Ivan Magill had received a similar posting, a fortuitous coincidence bringing these two men together. Their first meeting was in the office of the Commanding Officer and there began a lifelong friendship and pioneering partnership in the specialty they were about to enter. Initially they were told there was no place for them, but recalling a need for anaesthetists, the Commanding Officer offered them this option. Neither had any experience, nor could they have envisaged that together they would lay the foundation of the sophisticated tracheal techniques that would pave the way for such significant advances both in anaesthesia and surgery.

The surgery of wounds of the face and jaws presented a formidable challenge and the problems of providing adequate and safe anaesthesia were no less forbidding. Other military hospitals were treating similarly injured casualities, but at Sidcup these two young anaesthetists, with an enthusiastic flair for invention and encouraged by Gillies, brought innovation and progress to the limit of available facilities and knowledge. Their several contributions were complementary in the advancement of tracheal techniques.

Existing anaesthetic methods were, in one way or another, unsatisfactory. Oil/ether colonic anaesthesia allowed surgical access, but produced airway problems and prolonged unconsciousness often ensued. The method of choice was the insufflation of nitrous oxide/oxygen and ether via an intratracheal catheter, a method introduced by Elsberg, the New York neurosurgeon,[3] and brought to England by Kelly, a Liverpool surgeon,[4] in 1912. This technique guaranteed a safe airway and prevented the entry of blood into the trachea. The Shipway warm ether apparatus replaced the more primitive mechanism of delivering ether by hand or foot bellows, or by electric motor.

In 1919, Silk[5] described his wide-bore rubber pharyngeal airway. At Sidcup this was introduced as a return airway, allowing the ether-laden expired gases to be directed away from the surgeon and the pharynx to be packed. The tube was adapted for both nasal and oral use and metal adaptors were designed for both routes. To prevent damage to the nasal mucosa, the naris was dilated by the passage of graduated and lubricated tubes.[6] In this paper, Rowbotham records a chance blind intubation with the wired catheter and the subsequent consideration given to assessing the correct curve necessary for a successful attempt—'Occasionally when the catheter is passed through the nose . . . and pushed on, the cough characteristic of its passage into the trachea occurs and on inspection the fact that it has actually passed between the cords is confirmed. Working on this, attempts were made to judge the curve on the catheter required to direct its end towards the mid point of the thyroid cartilage'. The technique of blind nasal intubation thus emerged, a method now regrettably rarely taught or practised.

A further modification of the insufflation technique was the introduction of a second tube into the trachea, alongside the insufflating catheter, to give free and reliable respiration, or to and fro respiration using a large bore tube. An ingenious combination of tube and catheter is

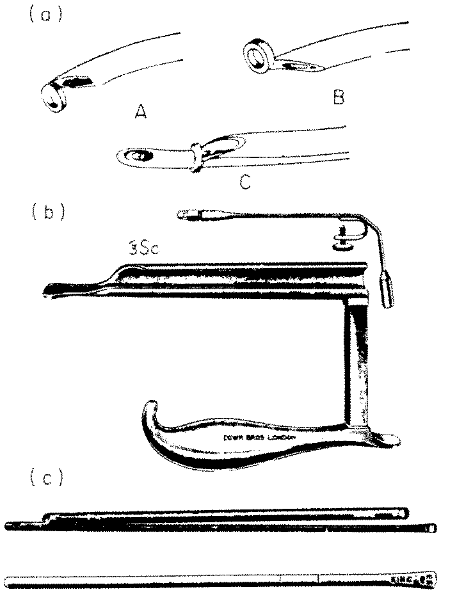


Fig. 2. (a) Rowbotham's modified two-tube tracheal method (1923). (A), end cut leaving a ring; (B), ring everted; (C), tube in place on catheter. (b) Magill's original pattern laryngoscope (*c*. 1920). (c) Magill and Rowbotham's double tracheal gum elastic catheter (1920). (By courtesy of the British Medical Journal.)

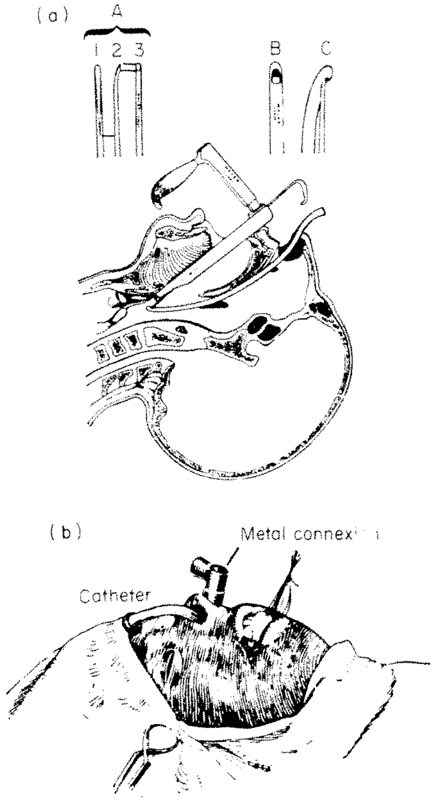


Fig. 3. (a) Rowbotham's method of passing a tracheal catheter with a Hill's laryngoscope. (b) The Rowbotham two-catheter method in use. (By courtesy of the British Medical Journal.)

described.[7] Magill described this 'double tube' method about the same time.[8]

Stanley Rowbotham more than once recalled that it was when performing laryngoscopy to insert the insufflating catheter that the sight of the Silk tube lying just above the glottis presented the idea of a simple wide-bore tracheal tube (personal communication). He records: 'It occurred to me that if one could pass a single tube of adequate size ... into the trachea and allow the patient to breathe backwards and forwards through it, a state of things much more akin to that which occurs during natural respiration would be achieved. Moreover, the first part of the respiratory passages would be just as well cut out',[9] a recognition of the importance of reducing the dead space. Magill records intubating a patient with a wide-bore tube in 1920.[10] It is clear that, at Sidcup, the use of wide-bore techniques was only occasional, insufflation remaining the method of choice for some years.

In a minority of cases, morphine premedication and local infiltration with procaine and adrenaline were combined with nitrous oxide anaesthesia, an application of Crile's anoci-association theory.[11] Whenever possible, Rowbotham visited University College Hospital to learn from Felix Rood, whom he recalled gratefully. (Personal communication).

When the importance of the tracheal technique was evident, Magill, in Rowbotham's words 'did the rounds of the rubber merchants selecting suitable tubing of graduated sizes'. These were stored in round tins to preserve the curves. The cut ends were rubbed smooth with a chloroform-soaked swab (Personal communication). The simplification and development of tracheal anaesthesia, now in universal use, was the ultimate achievement of Magill and Rowbotham.

After the Armistice, the Queen's Hospital was transferred to the Ministry of Pensions. The staff remained, Rowbotham and Magill becoming part-time at 4 days a week and taking up other part-time appointments. At this time, the surgeons at Sidcup were receiving £800 per annum,

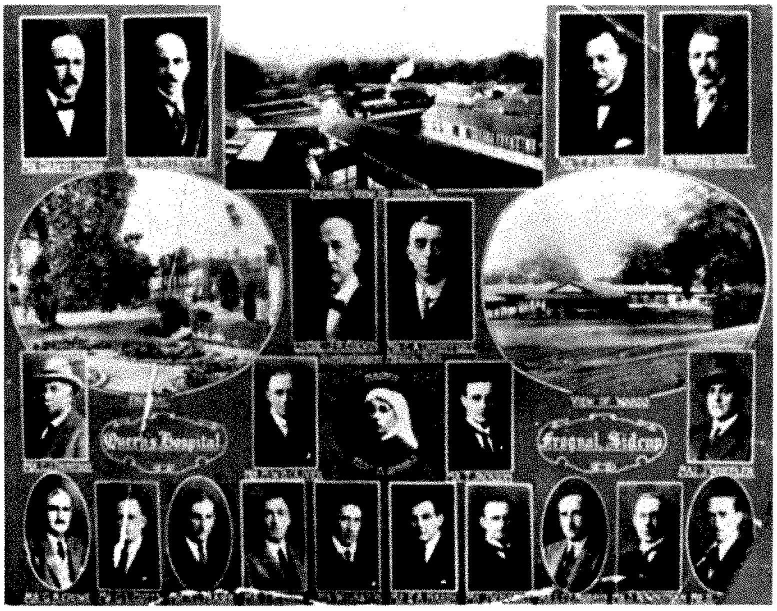


Fig. 4. Souvenir of the plastic surgery unit at Sidcup. (By courtesy of the Bexley Health Authority.)

the anaesthetists £750 per annum. An American plastic surgeon working there, J. Eastman Sheehan, failed to persuade Magill and Rowbotham to emigrate and become his anaesthetists. In due course, Rowbotham joined the staff of several hospitals, namely the Dreadnought Seaman's Hospital at Greenwich, St John's at Lewisham, the Gordon, The Royal Dental, the Westminster, the Royal Cancer (later the Royal Marsden), the Royal Free and Charing Cross Hospitals. These last three became his main appointments.

This was the era of the Voluntary Hospital, with consultants attending on an honorary basis, depending for their livelihood on private practice. Rowbotham, finding it difficult to make ends meet, as did many anaesthetists of the time, bought a partnership in general practice with a bank loan of £4000, which he repaid in 3 years. More importantly, he believed an anaesthetist should also be a physician and this allowed him to retain an interest in general medicine. In 1932 he obtained the MD (Durham) by examination.

Stanley Rowbotham was remarkably versatile and inventive. He designed an insufflation apparatus,[12] a chloroform vaporizer, a cuffed pharyngeal airway,[13] an introducer for lumbar puncture needles,[14] a special self-filling syringe and angled needles for local analgesia[15] and a laryngeal spray.[15] Use of the latter could well be revived to provide analgesia for nasotracheal fibreoptic bronchoscopy. In addition, he had a thorough knowledge of the techniques of local analgesia and had used every method described by Labat.[16] He became a pioneer of basal narcosis, first with rectal paraldehyde and then with Avertin.[17] When intravenous anaesthesia became practicable, he was to the fore using Nembutal. In early 1934 he was the first in the United Kingdom to use cyclopropane. The cylinders were given to him by a South African passing through London from America. Magill was invited to share the demonstration at Charing Cross.[18]

Dr Rowbotham's main anaesthetic activity at this time was with Cecil Joll, the well-known thyroid surgeon. It must be remembered that thyroidectomy was then a hazardous procedure, the antithyroid drugs having yet to be discovered. They were introduced into clinical practice in North America by Astwood in 1943.[19] Stanley Rowbotham successfully overcame the difficulties of the management of these patients, again with a combination of basal narcosis—the dosage carefully assessed on body weight and the basal metabolic rate, local analgesia and light general anaesthesia with nitrous oxide. After cocainisation using his nasal laryngeal spray, blind nasal intubation was performed. The local technique involved a superficial and deep infiltration of the neck, paying special attention to

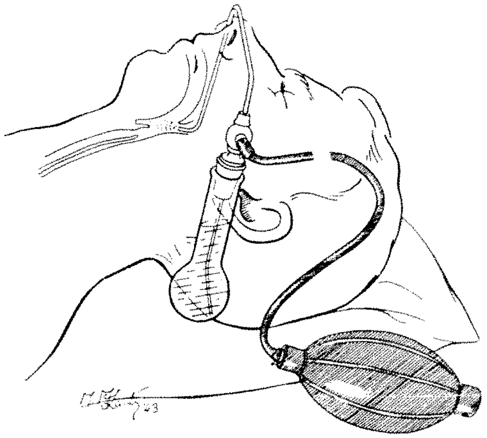


Fig. 5. Special spray in position for cocainizing the larynx. (By courtesy of the British Medical Journal.)

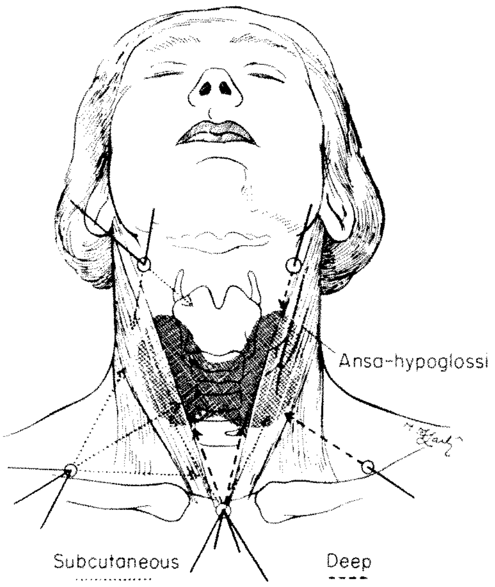


Fig. 6. Scheme of infiltration for thyroidectomy. (By courtesy of Blackwell Scientific Publications Ltd.)

blocking the ansa hypoglossi to relax the infrahyoid muscles. The procedure was facilitated by using the self-filling syringe of his own design, with his angled needles for approaching the goitre. Joll liked the patients to strain once the haemostatic sutures were inserted. This was achieved with one breath of ether. Wrist restraints permitted the necessary light level of anaesthesia. For a period, one thyroidectomy on each list was performed under local analgesia only.

From May 1941 to May 1944, 946 goitre operations using these techniques were performed at the Royal Free Hospital with 9 deaths, a remarkable record. Stanley Rowbotham described his accumulated experience in his book *Anaesthesia in Operations for Goitre*, an early anaesthetic monograph which remains worthy of study. In 1948 he was elected to honorary membership of the Royal College of Physicians in recognition of this work.

When World War II was declared, Rowbotham returned to the RAMC, in charge of a Surgical Division. He was later posted to the Cambridge Hospital at Aldershot to work with Edward Muir. There, in the Burns Unit, he successfully used intravenous procaine, intravenous amethocaine being found to be too toxic. He had charge there, also, of a School of Anaesthesia for Americans, who came in groups of twelve for a 3-week course. After the Normandy landings, he joined a facio-maxillary unit in Belgium, where his experience was invaluable.[20] An innovation here was the use of 1% bromethol in saline as an intravenous infusion for bronchoscopy, when bronchial toilet was indicated. His age and length of service were such that he was immediately demobilised after VE day. He received the Bronze Star of the US Forces.

Dr Rowbotham arrived back at Charing Cross and the Royal Free with Dr F. Prescott, then Clinical Research Director of Burroughs Wellcome and ampoules of purified *d*-tubocurarine chloride, the greatest advance in anaesthesia since 1846. Organe at Westminister Hospital collaborated in early pharmacological work, with Dr Prescott as a human volunteer.[21] These experiences were published, together with later clinical studies from Charing Cross and the Royal Free.[22] The favoured technique involved papaveretum and hyoscine premedication, thiopentone induction, nitrous oxide/oxygen anaesthesia with blind nasal intubation to ensure the airway at all times, tubocurarine chloride 0.4 mg/kg body weight intravenously; 30 minutes later, half the initial dose of relaxant was given intramuscularly. An ingenious attempt was made to measure muscle relaxation by a saline manometer with a perforated needle in the biceps, but this did not prove helpful. Respiration was assisted as indicated. Later, a mechanical ventilator was designed, consisting of two hinged wooden flaps which rhythmically squeezed the reservoir bag of the Waters 'to-and-fro' absorber. An electric motor provided the power and a pressure gauge was incorporated (de Saram M., personal communication). At this time, Rowbotham was in contact with Dr R. Beaver and information on early ventilators was exchanged.

The centenary of the introduction of anaesthesia occurred in 1946, and Stanley Rowbotham was elected President of the Section of Anaesthesia of the Royal Society of Medicine. His presidential address was a review of the main events in anaesthesia during the century.[23]

In addition to his busy clinical practice, Rowbotham organised teaching sessions for junior anaesthetic staff, introducing outside speakers—Professor R.R. Macintosh spoke on the Oxford vaporizer, Dr W.W. Mushin on nerve blocks for E.N.T. surgery and Dr G.S.W. Organe on *d*-tubocurarine chloride. His ambition was to establish a Department of Anaesthesia at the Royal Free Hospital. Unhappily, this was not fulfilled in his time. There is now a biennial eponymous lecture by which he is commemorated.

Stanley Rowbotham appears not to have played a prominent part in the early affairs of the Association of Anaesthetists (Weller R., personal communication). When the Faculty of Anaesthetists was established within the Royal College of Surgeons in 1947, Rowbotham was nominated to serve on the original Board. This was a key moment in anaesthetic history. The National Health Service was about to be set up and it was important and by no means certain that anaesthesia would receive equality with other specialties, particularly the grading of anaesthetists as consultants. This the Faculty achieved. Present day critics of the Faculty and advocates of an independent organisation often fail to remember the debt that is owing to this body for the vision of these pioneers. Having served his initial term, in 1951 Dr Rowbotham was elected by the Fellows for a second term, the other successful candidates being Dr A. Marston and Dr R. Woolmer.

He retired in 1955, first to the Sussex coast at Seaford and then to Madeira. In 1958 he was elected an Honorary Fellow of the Faculty of Anaesthetists. During Professor Mushin's term of office as Dean of the Faculty, a dinner in Dr Rowbotham's honour was given at the Royal College of Surgeons. The speakers included Sir Arthur Porritt, President of the College, Sir Ivan Magill, Dr Ronald Jarman and Dr Katharine Lloyd-Williams.

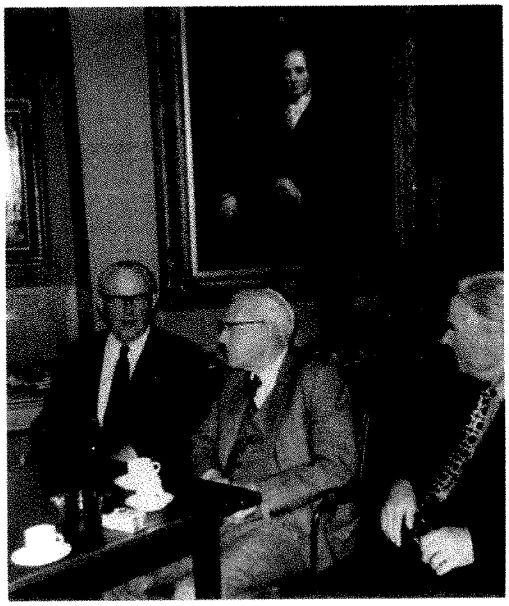


Fig. 7. Dr Stanley Rowbotham (centre), Sir Ivan Magill (left) in their retirement. Photographed at the Royal Society of Medicine with Dr K. Bryn Thomas.

In his last years, he suffered increasingly severe angina and deterioration of vision. Despite this, he continued to enjoy a full life, delighting in the company of friends and the entertainment of visitors to the island. Music too remained a great comfort. He retained the keenest interest in medicine and the progress of anaesthesia, the journals he received being read to him by his wife. He died on 10th April 1979 aged 88 years.

Acknowledgments

We are grateful to the Bexley Health Authority for permission to publish the Sidcup photograph from their archives. The Editor of the British Medical Journal and Blackwell Scientific Publications Ltd have each given permission to publish certain diagrams. Professor W.W. Mushin, Dr H.L. Thornton, Dr M. de Saram, Dr R. Weller and Dr S.R. Reynolds, a former Dean of Charing Cross Hospital Medical School, have assisted in various ways. The manuscript has been read by Dr J.A. Lee to whom we are indebted for helpful comments and additions to the text. Mrs M. Rowbotham, Dr Rowbotham's widow, has kindly indicated her approval of this project.

References

1. GRAY TC. Waterton Symposium (Correspondence). *British Journal of Anaesthesia* 1983; **55:** 1041.
2. DR BIRLEY'S NERVE SYRUP. Library of Pharmaceutical Society of Great Britain.
3. ELSBERG CA. Clinical experiences with intratracheal insufflation (Meltzer) with remarks upon the value of the method for thoracic surgery. *Annals of Surgery* 1910; **52:** 23–9.
4. KELLY RE. Anaesthesia by the intratracheal insufflation of ether. *British Medical Journal* 1912; **3:** 112.
5. SILK JFW. Anaesthetics: a nasal airway. *Lancet* 1919; **1:** 1030.
6. ROWBOTHAM S. Intratracheal anaesthesia by the nasal route for operations on the mouth and lips. *British Medical Journal* 1920; **2:** 590–1.
7. ROWBOTHAM ES. Laryngeal intubation in anaesthesia. *British Medical Journal* 1923; **2:** 1090–1.
8. MAGILL IW. The provision for expiration in endotracheal insufflation anaesthesia. *Lancet* 1923; **2:** 68–9.
9. ROWBOTHAM S. Intratracheal anaesthesia. *Lancet* 1926; **2:** 583–4.
10. MAGILL IW. Endotracheal anaesthesia. *Proceedings of the Royal Society of Medicine* 1928; **22:** 83–7.
11. CRILE GW. Phylogenetic association in relation to certain medical problems. *Boston Medical and Surgical Journal* 1910; **163:** 893–904.
12. THOMAS KB. *The Development of Anaesthetic Apparatus*. Oxford: Blackwell, 1975, pp. 189–90.
13. ROWBOTHAM ES. An inflatable pharyngeal tube. *Lancet* 1944; **2:** 15–16.
14. ROWBOTHAM S. Introducer for spinal needles. *Lancet* 1942; **1:** 734.
15. ROWBOTHAM E. *Anaesthesia in Operations for Goitre*. Oxford: Blackwell, 1945, pp. 67.
16. LABAT G. *Regional Anaesthesia: Its Technique and Clinical Application*. Philadelphia: Saunders, 1922.
17. ROWBOTHAM ES. Preliminary medication in anaesthetics. *Proceedings of the Royal Society of Medicine* 1929; **22:** 653–8.
18. ROWBOTHAM S. Cyclopropane anaesthesia. A report based on 250 cases. *Lancet* 1935; **2:** 1110–3.
19. ASTWOOD EB. Treatment of hyperthyroidism with thiourea and thiouracil. *Journal of the American Medical Association* 1943; **122:** 78–81.
20. THORNTON HL, ROWBOTHAM S. Anaesthesia in a maxillo-facial surgical unit with the British Liberation Army. *Anesthesiology* 1945; **6:** 580–96.
21. ORGANE G. The introduction of muscle relaxants. Audio cassette of *'Lest We Forget'*-2 meeting at the Royal Society of Medicine 1979 in the possession of the Association of Anaesthetists.
22. PRESCOTT F, ORGANE G, ROWBOTHAM S. Tubocurarine chloride as an adjunct to anaesthesia. Report on 180 cases. *Lancet* 1946; **2:** 80–4.
23. ROWBOTHAM S. A hundred years of anaesthesia. *Anaesthesia* 1947; **2:** 86–92.

Anaesthesia, 1986, Volume 41, pages 53–56

CASE REPORT

Phenelzine poisoning

F. X. BREHENY, G. J. DOBB AND G. M. CLARKE

Summary

A 46-year-old female with severe phenelzine poisoning was managed successfully by alpha blockade and fluid loading, with the aid of invasive haemodynamic monitoring. The pathophysiology was documented, showing elevated plasma and urinary catecholamines, cardiovascular abnormalities and a contracted blood volume. Most of these changes were reversed following treatment.

Key words

Ataractics; monoamine oxidase inhibitors.
Intensive care.

Self-poisoning with tricyclic antidepressants is the most common cause of drug overdose in patients requiring admission to our intensive care unit (ICU). Monoamine oxidase inhibitors (MAOIs) are enjoying a revival as antidepressant agents, despite their well known interactions with other drugs and foods. If this trend continues, self-poisoning with MAOIs may occur more often in admissions to ICU. A patient who had taken an overdose of Phenelzine recently presented to the Royal Perth Hospital and required full supportive measures to assure a satisfactory outcome.

Case history

A 46-year-old female was brought unconscious to the Emergency Centre of our Hospital. She had a 2-year history of psychiatric depression, treated initially with imipramine, and more recently with phenelzine. A few hours before presentation, she had ingested an unknown quantity (probably about 60) of phenelzine 15 mg tablets.

Examination at the time of presentation revealed a comatose middle aged female. She made no purposeful responses to painful stimuli, had a poor gag reflex, normal pupils and pupillary reflexes, and had flaccid limbs with absent reflexes. She had a pulse of 72/minute, and an arterial blood pressure of 150/100 mmHg, with normal heart sounds. Electrocardiography showed non-specific flattening of the T-waves with poor progression of the R-waves over the anterior chest leads. A chest X ray showed changes consistent with pulmonary aspiration on the right side. Her peripheries were warm and well perfused.

In view of the inability to protect her airway, her trachea was intubated prior to gastric lavage, which did not reveal any tablet remnants. After instillation of 50 g activated charcoal, she was

---

F.X. Breheny, MB, BCh, BAO, FFARCSI, FFARACS (Intens), Senior Registrar, G.J. Dobb, MSc, MB, BS, MRCP, FFARCS, Specialist in Intensive Care, G.M. Clarke, MB, BS, FFARCS, FFARACS, Director of Intensive Care, Royal Perth Hospital, Perth, Western Australia, 6001.
Correspondence should be addressed to F.X. Breheny, Director of Intensive Care, Fremantle Hospital, Alma Street, Fremantle, 6160, Western Australia.

0003–2409/86/010053 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

transferred to the ICU for further management. On admission to the ICU, she was deeply unconscious and hypothensive. Initial treatment included intermittent positive pressure ventilation of her lungs (IPPV) and fluid loading to a central venous pressure (CVP) of 10 cm H_2O with a total of 300 ml of 0.9% sodium chloride, and 300 ml of stable plasma protein solution (SPPS). After the onset of spontaneous ventilation, she was allowed to breathe humidified oxygen enriched air via a T-piece system, while remaining intubated. Ten hours after admission, she developed cold, clammy peripheries, while core body temperature remained normal. Arterial blood pressure was low at 80/50 mmHg and failed to respond to increments of SPPS (total 350 ml). She developed a sinus tachycardia (120–130/minute), profuse sweating, mainly of the head, neck and upper limbs, with excessive salivation and bronchorrhoea. She became restless and agitated, especially when stimulated, thus making nursing care very difficult.

Four hours later, her breathing became more laboured, arterial blood gases deteriorated, and a chest X ray revealed florid pulmonary oedema. After restarting intermittent positive pressure ventilation with 5 cm H_2O of positive end-expiratory pressure (PEEP), she underwent a spontaneous diuresis with rapid clearing of the pulmonary oedema.

There was little change over the next 36 hours. She required a constant alphaxalone/alphadalone (Althesin) infusion for sedation, in order to allow proper nursing care. She remained hypotensive, had a persistent tachycardia, and cold, clammy peripheries, and continued to sweat profusely. When dopamine was given in a dose of 1 μg/kg/minute to support the blood pressure, there was an exaggerated response, with the systolic blood pressure rising from 80 mmHg to 180 mmHg. Atropine 1.2 mg had no effect on any of the signs. Phentolamine 5 mg administered by slow intravenous infusion, resulted in a slow transient fall in the systolic blood pressure to 60 mmHg.

On the third day, a Swan-Ganz catheter was inserted because of persisting hypotension and abnormal peripheral perfusion. This revealed an initial pulmonary artery wedge pressure (PAWP) of 11 mmHg, with a very high systemic vascular resistance (SVR) (Table 1). Alpha adrenergic blockade and a colloid infusion (SPPS) were commenced simultaneously. Phentolamine 40 mg administered over 10 hours, was followed by the institution of prolonged alpha blockade by administering 75 mg of phenoxybenzamine over a 4-hour period. The same dose of phenoxybenzamine was repeated 3 days later. Serial haemodynamic measurements showed a decreasing SVR and an increasing cardiac index.

Tables 2 and 3 record the plasma and urinary catecholamines. Plasma catecholamines were measured using a radio-enzymatic assay and urinary catecholamines were measured using the trihydroxyindole technique, following separation using a weak cation-exchange resin. Measurements of blood and plasma volumes (using the I^{125} labelled albumin technique) were carried out on two occasions, one week apart, before and after alpha adrenergic blockade (Table 4).

Table 1. Haemodynamic measurements before and after alpha blockade

	CI*	SVR†	PVR‡	PAWP§	CVP‖	HR¶	BP**	SPPS††
Pre-alpha blockade	2.7	27.6	1.9	7	6	120	130/95	
Alpha blockade† 3 hours	3.4	18.1	1.3	12	15	115	135/90	700
Alpha blockade† 6 hours	3.6	13.4	0.9	13	15	112	115/75	1500
Alpha blockade† 3 days	4.5	9.9	1.0	14	9	111	101/62	
Normal range	2.8–3.6	11.2–15.0	1.0–1.5	5–11				

*Cardiac Index l/sq m.

†Systemic vascular resistance, mmHg/(litres/min).

‡Pulmonary vascular resistance, mmHg/(litres/min).

§Pulmonary artery wedge pressure, mmHg.

‖Central venous pressure.

¶Heart rate.

**Blood pressure, mmHg.

††Stable plasma protein solution.

Table 2. Urinary catecholamine levels

Day after admission	Catecholamines µmol/l	Normetadrenaline µmol/l
2	3.9	15
5	2.1	7.4
9	—	2.7
Reference	7	
range	< 1.5	< 6.0

Alpha adrenergic blockade was instituted on the third day after admission.

There was a marked clinical improvement in peripheral perfusion which paralleled the improvement in the haemodynamic measurements (Table 1). The tachycardia persisted and the patient remained restless and agitated when sedation was temporarily ceased. Both of these resolved spontaneously over the next 3 days.

Table 3. Plasma catecholamine levels

Day after admission	Noradrenaline ng/ml	Adrenaline ng/ml	Dopamine ng/ml
2	2.39	2.12	19.7
5	2.17	1.25	10.89
9	1.61	0.04	0.29
21	0.76	0.05	0.027
Reference	0.1–0.4	< 0.05	~0.05

Discussion

The features of MAOI poisoning are due to the tissue accumulation of catecholamines rather than a direct toxic effect of the drug. There is usually a delay of 6–12 hours before the onset of signs of poisoning. The characteristic features are hyperpyrexia, hypertension, and central nervous system stimulation with restlessness and, sometimes, seizures. The peripheral tone is increased and reflexes are brisk. Hyperhidrosis and horripilation are also commonly seen. Hypotension is a poor prognostic sign, which often occurs late and most often follows pure MAOI overdose.[1]

Table 4. Blood volume measurements

Day after admission	Plasma volume (ml)	Blood volume (ml)
2	1970	3012
9	3012	4317
Predicted	2284	3600–3800

In the case reported, in the region of 900 mg of phenelzine was ingested, a dose which is within the range in which death has been reported to occur.[2] After a 6–12 hour delay, presenting signs included an altered conscious state, restlessness and peripheral vasoconstriction. This was followed by hypotension, excessive secretions, hyperhidrosis and tachycardia. It may be speculated that the pulmonary oedema was precipitated by an abrupt increase in left ventricular afterload causing excessive strain on the left ventricle, aggravated by generous, though not excessive, intravenous fluids. The rapid clearing of the pulmonary oedema following sedation, tracheal intubation and assisted ventilation supports this thesis.

Not all of the clinical features could be accounted for by an excess of catecholamines alone. The copious salivation and bronchorrhoea were more like acetylcholine excess and hypotension, rather than hypertension, was a feature despite peripheral vasoconstriction. The absence of hyperpyrexia, which is a characteristic of severe poisoning and a leading cause of death, is not easily explained, although it may occur more commonly when other antidepressant agents are ingested at the same time.[3] Althesin was used for sedation because of its efficacy in the critically ill.[4] Administration by infusion allowed reassessment of the patient's conscious state soon after it was stopped; it is no longer available.

The concentrations of both urinary and plasma catecholamines were markedly elevated and are similar to those in patients with phaeochromocytomata. Measurement of the blood and plasma volumes clearly show the presence of a contracted blood volume before alpha adrenergic blockade.

The features of MAOI poisoning are essentially those of catecholamine excess, so treatment should counter these effects with alpha and beta adrenergic blockade. As the alpha adrenergic effects were the most prominent, alpha blockade was instituted first, with beta blockade to follow if it was necessary. The rapid fall in blood pressure after a trial of phentolamine and the recent pulmonary oedema suggested that alpha adrenergic blockade and fluid loading could be more safely performed with invasive haemodynamic monitoring. This allowed volume loading and vasodilatation to be performed concurrently. The improvement (shown in Table 1) in both cardiac output and systemic vascular resistance after 700 ml of SPPS and 20 mg of phentolamine was also apparent clinically. The continued improvement and its maintenance with phenoxybenzamine are evident from subsequent measurements. The progress was such that beta blockade was not considered necessary.

This case report demonstrates some of the biochemical and haemodynamic alterations which occur secondary to phenelzine poisoning. Whereas the clinical features have been described before,[1,2,5] the biochemical and cardiovascular consequences have not been well recorded. Treatment along physiological and pharmacological lines proved successful. Continued support is necessary until adequate amounts of new monoamine oxidase is regenerated. This is said to occur in 10 days to 2 weeks.[6] This case suggests, however, that active therapy does not necessarily have to be continued for this length of time. Clinical signs of poisoning were not present but the level of noradrenaline had not returned to normal after 21 days, which indicates the prolonged effect of phenelzine on MAO inhibition. The use of chlorpromazine, which produces mild alpha blockade as well as central depression and has a hypothermic effect, has previously been successfully used for MAOI poisoning.[7,8] We did not use it, but it might have been useful.

Our recommendations for the future management of poisonings with MAOIs would be: standard methods for drug overdose;[9] if significant poisoning is confirmed, chlorpromazine in doses up to 50–100 mg may alleviate the symptoms and signs; more severe poisoning may require insertion of a pulmonary artery catheter and alpha blockade while the haemodynamic response is monitored, if tachycardia and dysrhythmias are a problem, beta blockade with intravenous practolol or propranolol would be indicated; if hyperpyrexia is not alleviated by these measures, active cooling should be undertaken.

Acknowledgments

We would like to thank the University Department of Medicine of Royal Perth Hospital for the measurements of plasma catecholamine levels.

References

1. Guzzardi L. Monoamine oxidase inhibitors. In: Haddad LM and Winchester J. (eds) *Clinical management of poisoning and drug overdose*. Philadelphia: Saunders, 1983: 596–602.
2. Davis JM, Bartlett E, Termini BA. Overdosage of psychotropic drugs: A Review. Part II: Antidepressants and other psychotropic agents. *Diseases of the Nervous System*. 1968; **29:** 246–56.
3. Ciocatto E, Fagiano G, Bava GL. Clinical features and treatment of overdosage of monoamine oxidase inhibitors and their interaction with other psychotropic drugs. *Resuscitation* 1972; **1:** 69–72.
4. Stewart GO, Dobb GJ, Craib IA. Clinical trial of continuous infusion of alphaxalone/alphadolone in intensive care patients. *Anaesthesia and Intensive Care* 1983; **11:** 107–12.
5. Crome P. Antidepressant overdosage. *Drugs* 1982; **23:** 431–61.
6. Goodman L, Gilman A (eds). *The pharmacological basis of therapeutics*. 6th Edn. New York: MacMillan, 1980. 428.
7. Reid DD, Kerr WC. Phenelzine poisoning responding to phenothiazine. *Medical Journal of Australia* 1969; **2:** 1214–5.
8. Robertson JC. Recovery after massive MAOI overdose complicated by malignant hyperpyrexia, treated with chlorpromazine. *Postgraduate Medical Journal*. 1972; **48:** 46–65.
9. Wright RC. A simple plan for the management of drug overdosage. *Anaesthesia and Intensive Care* 1974; **4:** 288–302.

Anaesthesia, 1986, Volume 41, pages 57–59

CASE REPORT

Acute upper airway obstruction

Spontaneous retropharyngeal haematoma in a patient with polycythaemia rubra vera

J. W. MACKENZIE AND JILLIAN A. JELLICOE

Summary

A case is described of retropharyngeal haematoma due to spontaneous bleeding from the inferior thyroid artery and causing acute upper airway obstruction. Results of the haematological investigations were suggestive of underlying polycythaemia rubra vera. The presentation and findings in this case are discussed.

Key words

Complications; airway obstruction.
Blood; polycythaemia rubra vera.

Retropharyngeal haemorrhage is rare,[1] usually due to trauma or surgery in the neck, and is an uncommon cause of respiratory obstruction. The diagnosis is straightforward once it has been considered, and prompt intervention may be lifesaving. Spontaneous bleeding may occur in polycythaemia rubra vera, but this condition alone has not previously been described as a cause of retropharyngeal haematoma.

Case history

A 72-year-old woman was admitted for social reasons precipitated by the illness of her husband. She was known to be on antihypertensive medication (Navidrex-K one tablet daily, and methyl dopa 250 mg t.d.s.), and to have sustained a cerebrovascular accident 8 years previously. She had no complaints on the day of admission; her daughter thought that the patient might have fallen at home, but there was no evidence of any injury. Her arterial blood pressure was 150/80 mmHg and signs of an old left hemiparesis were present. However, routine haematological investigations were suggestive of polycythaemia rubra vera.

The following afternoon she developed sudden symmetrical swelling of her neck, causing pain and slight distress. The swelling was firm, non-pulsatile, about 6 cm in diameter and had the appearance of a goitre. At this stage respiration was not compromised and pulse and blood pres-

---

J.W. Mackenzie, MB, BCh, MRCP, Senior Medical House Officer, Poole General Hospital, Jillian A. Jellicoe, LRCP, MRCS, FFARCS, Senior Registrar in Anaesthetics, Poole General Hospital, Longfleet Road, Poole, Dorset.*

*Present address: Consultant Anaesthetist, Shackleton Department of Anaesthetics, Southampton General Hospital.

Correspondence to: Dr J.W. Mackenzie, Department of Anaesthetics, St Thomas' Hospital, London SE1 7EH please.

0003–2409/86/010057 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

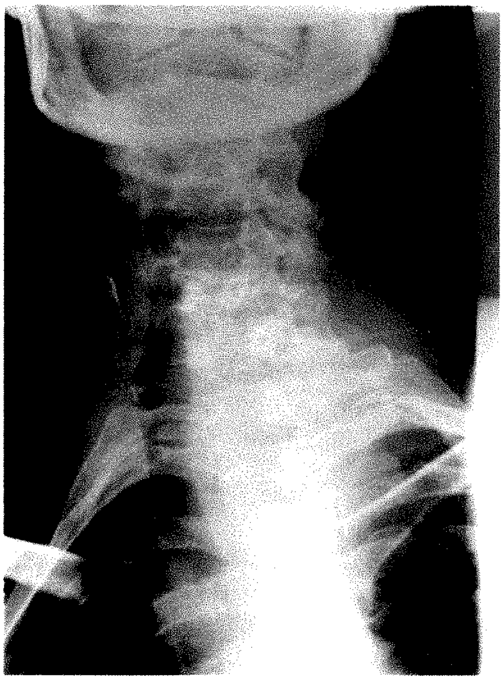


Fig. 1. Soft tissue X ray at time of appearance of swelling in the neck. A mass behind the trachea is displacing it to the right.

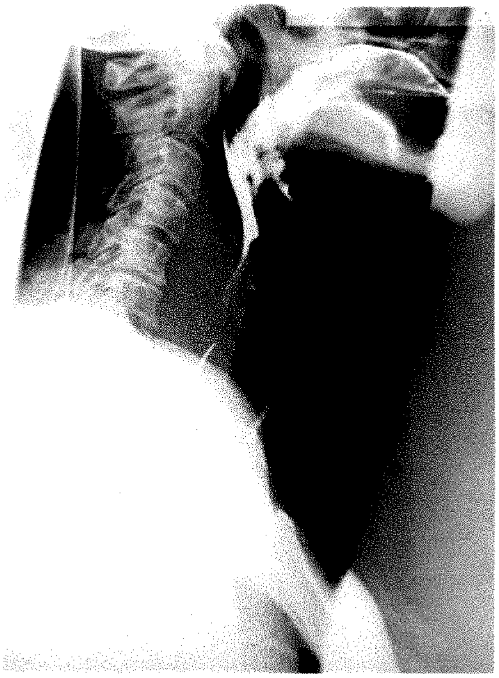


Fig. 2. Barium swallow confirms presence of a mass compressing the oesophagus.

sure readings were unchanged. Soft tissue X rays performed at this time showed a mass behind the trachea, displacing it to the right (Fig. 1). A barium swallow confirmed that the mass lay behind and compressed the oesophagus (Fig. 2).

Two hours after the initial event, the patient complained of more pain, at which time the cervical swelling rapidly increased and she became extremely distressed and dyspnoeic. It was obvious at this stage that respiration was becoming rapidly obstructed and the trachea was therefore intubated as an emergency to maintain the airway. At laryngoscopy, the cords were seen to be deviated to the right, but a 7.5 mm tube could not be passed. Fortunately, a 6.0 mm cuffed Portex tube could be passed with relative ease and blood gas analysis following intubation and ventilation was satisfactory. The swelling was now asymmetric, more predominant on the left, and needle aspiration here revealed fresh blood. The patient was kept sedated, paralysed and ventilated prior to transfer to theatre, where the neck was explored via a thyroid collar incision. A large retropharyngeal haematoma was found and the bleeding point identified as the left inferior thyroid artery, which was ligated. No aneurysm was apparent and the thyroid itself appeared normal.

In view of the probability of laryngeal oedema postoperatively, the patient's lungs were ventilated for 4 days, when it was possible to change the tracheal tube to a size 8.0 mm to permit spontaneous ventilation. However, the patient's level of consciousness remained depressed and ventilation was continued until the next day, when signs of shock developed and resuscitative measures were unsuccessful.

Postmortem examination revealed massive haemoperitoneum, an enlarged spleen (1.6 kg) in which infarction had occurred, together with thrombosis of the splenic vein, presumably leading to splenic rupture and the terminal signs of shock. There was no evidence of septicaemia.

Discussion

The retropharyngeal space in the neck is a potential space anterior to the prevertebral fascia but behind the oesophagus. Inferiorly, the space continues into the superior mediastinum. A full anatomical description is given by Sandor and Cooke.[2]

The clinical diagnosis of retropharyngeal haemorrhage may be inferred from the following triad: symptoms of acute superior mediastinal compression; radiographic displacement of the trachea anteriorly (the distance between the anterior part of the body of C_2 and the posterior wall of the pharynx should not normally exceed 7 mm); bruising of the neck, tracking to the anterior chest wall within 48 hours. Causes include trauma (which may be minimal, e.g. coughing), surgery (especially thyroid), erosion of the carotid artery by retropharyngeal abscess, rupture of a carotid aneurysm, extension of bleeding from an aortic aneurysm and spontaneous rupture in patients on anticoagulants, and those with aberrant arteries at the level of the thoracic inlet.[2]

Thrombotic complications are common in polycythaemia rubra vera, but a bleeding tendency has also been noted; the precise cause of this tendency remains uncertain.[2-4] Multiple minor and often contradictory anomalies in clotting factors have been observed but the major role in haemorrhagic episodes is considered to lie with defective platelet function.[5]

A search of the literature has revealed surprisingly few episodes of spontaneous bleeding in polycythaemia rubra vera; a 55-year-old, previously fit but undiagnosed patient developed a groin haematoma and was subsequently diagnosed as having polycythaemia vera.[6] Owens *et al.* describe two patients on anticoagulants, including a 61-year-old man on warfarin for polycythaemia vera who developed neck swelling after a violent tussive episode. Interestingly, in this case, the prothrombin time ratio was not prolonged, so the bleeding tendency may have been due to the polycythaemia itself. Genovesi and Simmons describe a similar patient, also on anticoagulants, in whom clotting times were prolonged.[8]

The haematoma usually resolves within 7–14 days and respiratory embarrassment is not usually a problem. If it is, O'Neill *et al.*[9] recommended tracheostomy under local anaesthesia to gain control of the airway in elderly patients, since intubation may be difficult and can lead to rupture of the trachea. clearly, in this case, tracheostomy was not possible and tracheal intubation immediately relieved the obstruction to respiration, but in either procedure difficulties may be encountered due to the effects of a large haematoma on normal anatomical arrangements.[10]

Conclusions

A 72-year-old woman with probable polycythaemia rubra vera developed a retropharyngeal haematoma, leading to respiratory obstruction 30 hours after a social admission to hospital. There was a possibility that she had fallen at home, but this was not confirmed by the history and there was no evidence of injury. The haematoma was found to be due to an apparently spontaneous haemorrhage from the left inferior thyroid artery. She subsequently died from intraperitoneal haemorrhage, due to thrombosis and rupture of an enlarged spleen. Spontaneous bleeding in unusual sites may be due to underlying polycythaemia rubra vera.

Acknowledgements

The authors wish to thank Dr P. Clein, Consultant Physician, for permission to present this patient. Thanks to Mrs R. Sealey for typing this paper.

References

1. Irvine GH. Retropharyngeal haemorrhage. *British Journal of Surgery* 1984; **71:** 320–1.
2. Sandor F, Cooke RT. Spontaneous cervicomediastinal haematoma. *British Journal of Surgery* 1964; **51:** 682–6.
3. Lewis SM, Szur L, Hoffbrand AV. Thrombocythaemia. *Clinics in Haematology* 1972; **1:** 339–57.
4. Gunz FW. Hemorrhagic thrombocythemia. A critical review. *Blood* 1960; **15:** 706–23.
5. Wetherley-Mein G, Pearson TC. The myeloproliferative disorders. In: Hardisty R.M. and Weatherall D.J., eds. *Blood and its disorders* 2nd ed. Oxford: Blackwell Scientific Publications, 1982: 1269–1316.
6. Askew A. Spontaneous bleeding in polycythaemia vera. *Medical Journal of Australia* 1980; **2:** 456.
7. Owens DE, Calcaterra TC, Aarstad RA. Retropharyngeal hematoma. A complication of therapy with anticoagulants. *Archives of Otolaryngology* 1975; **101:** 565–8.
8. Genovesi MG, Simmons DH. Airway obstruction due to spontaneous retropharyngeal hemorrhage. *Chest* 1975; **68:** 840–2.

Anaesthesia, 1986, Volume 41, pages 61–66

CASE REPORT

Detection of neurological damage during cardiopulmonary bypass

S. N. C. BOLSIN

Summary

Three cases of neurological damage, which occurred during cardiopulmonary bypass, and which were detected by the cerebral function analysing monitor, are reported. A fourth case, which had similar changes on the cerebral function analysing monitor but no neurological damage, is also described. The importance of changes in frequency of the cerebral electrical activity in the early detection and accurate prediction of severity of neurological damage is emphasised. The advantages of this instrument over other displays of the electroencephalogram are discussed.

Key words

Brain; electroencephalography.
Complications; neurological.

Despite an overall improvement in the results of open heart surgery (OHS), reports of neurological damage continue to appear.[1,2] The use of the cerebral function monitor (CFM) during cardiopulmonary bypass (CPB) is now well established and has been associated with a reduced incidence of neurological dysfunction detected postoperatively.[3,4]

High accuracy of prediction of neurological outcome has been claimed with the use of the CFM, but this can be attributed in part to the inclusion of a large number of unremarkable traces recorded from patients who eventually recovered.[5] The value of the CFM is also limited by the generation of both false positive records (an altered CFM trace associated with no apparent neurological deficit postoperatively) and false negative traces, where an uninterrupted CFM trace belies the occurrence of CNS damage detected later. This limitation of the CFM may be due to the lack of frequency information displayed in the record, which has been seen as a major drawback to its use.[6]

A new microprocessor-based instrument for the analysis and recording of cerebral electrical activity, the cerebral function analysing monitor (CFAM), has been developed.[7] The signal is received from biparietal surface electrodes, secured to the scalp with collodion, and the recording is made at a paper speed of 5 mm/minute. The CFAM provides similar information to the CFM but, in addition, generates a permanent record of frequency analysis of the filtered and augmented electroencephalogram (EEG) signal. Frequency analysis is in the classical bands (beta: 13–27 Hz; alpha: 7.5–13 Hz; theta: 3.5–7.5 Hz; delta: 1–3.5 Hz) and the record shows percentage of total electrical activity occur-

---

S.N.C. Bolsin, BSc, FFARCS, Research Registrar, Anaesthetic Department, Brompton Hospital, Fulham Road, London SW3 6HP.

0003–2409/86/010061 + 06 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

ring in each waveband. The CFAM also records the mean, 10th and 90th centiles of cerebral electrical activity, as well as the minimum and maximum excursions in a 2-second epoch.

The following four patients were in a study group of 30 patients monitored with the CFAM throughout operation and who were followed up with neurological examinations and a questionnaire. They are presented to demonstrate the predictive value of frequency analysis of the recorded signal. The CPB circuit for all cases included a BOS-10s oxygenator with a 40 micron arterial-line filter (Pall) for the first, second and fourth patients. No arterial line filter was used in the third patient.

Case histories

First patient

A 62-year-old man who required elective coronary artery vein grafting, showed a reduction in mean cerebral electrical activity at an early stage during CPB and at the unusually high temperature of 34°C. However, the most prominent change occurred in the frequency distribution, with complete loss of beta activity and marked reduction in alpha activity. There was a concomitant increase in the theta and delta wavebands. These changes were prolonged, lasting for 3 minutes, but subsequently recovered spontaneously. The mean arterial pressure was above 60 mmHg throughout this period and all other haemodynamic variables were normal. The CFAM record showed no other deterioration for the remainder of the operation. The total CPB time was 147 minutes.

This patient was found postoperatively to have suffered a mild right hemiparesis which resolved in 5 days. However, he did complain of vivid dreaming, blurring of vision and reduced concentration before discharge at 8 days. A follow up questionnaire at 6 weeks revealed that he now required glasses for near vision, had occasional double vision, had noticed a reduction in short term memory and was prone to uncharacteristic depression and emotional lability.

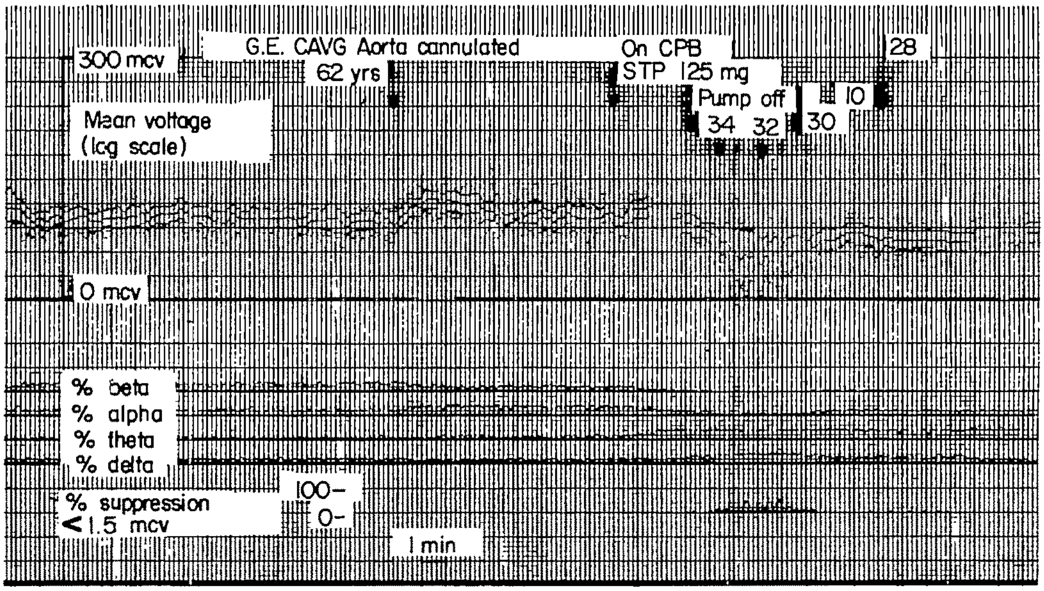


Fig. 1. The CFAM record of the first patient. The upper trace shows (from above) the maximum excursion, 90th centile, mean, 10th centile and minimum excursion of the processed amplitude signal in each 2-second epoch. The lower trace shows the percentage of activity in each of the EEG wavebands and the time the amplitude trace is depressed below 1.5 mcV for each 2-second epoch. Arrows indicate cannulation of the aorta, commencement of cardiopulmonary bypass (on CPB), the administration of sodium thiopentone (STP 125 mg), cessation of extracorporeal circulation for 10 seconds (pump off 10″) and degrees Centigrade (34, 32 & 30). The trace shows depression of the mean amplitude of the processed electroencephalogram with widening of the 10th–90th centile envelope. There is a marked shift from the faster frequencies (beta and alpha) to the slower frequences (theta and delta), with suppression of the mean amplitude below 1.5 mcV.

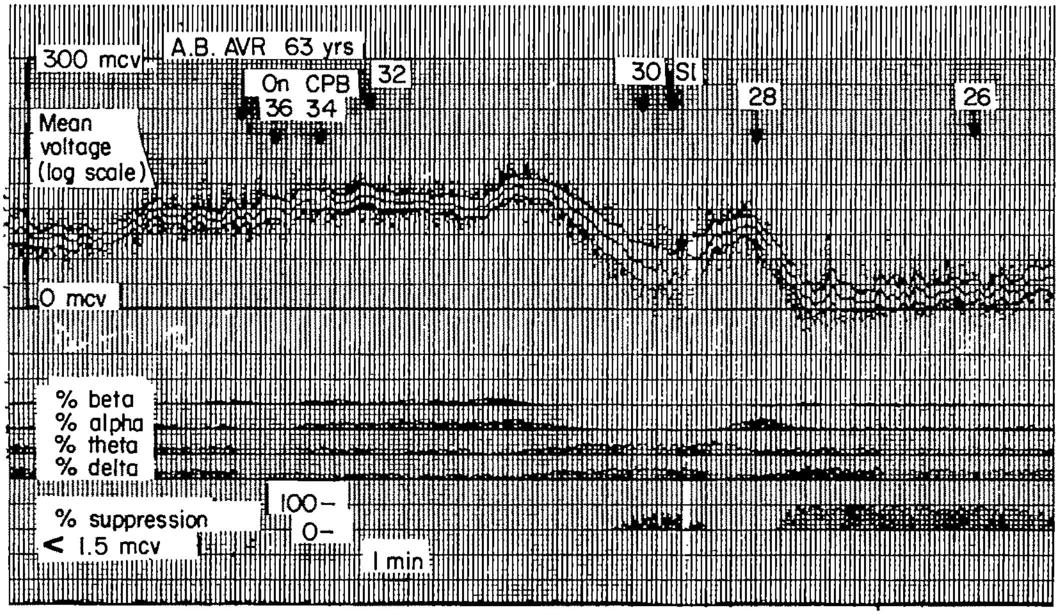


Figure 2. The CFAM record of the second patient. Format and labelling as for Fig. 1. The trace shows marked reduction of the mean voltage of the processed EEG and widening of the 10th–90th centile envelope with marked slowing of the frequency distribution. The surgeon was informed (SI) and adjustment of the aortic cannula produced a rapid improvement with restoration of the faster frequencies and increase in the mean voltage.

Second patient

A 63-year-old man with aortic stenosis who needed valve replacement gave a history of a single episode of collapse with loss of consciousness more than one year pre-operatively. During CPB, changes developed in the CFAM trace inconsistent with the temperature (32°C) and apparently normal perfusion, as judged by pump flow, perfusion pressure and arterial blood gas tensions. The changes observed were a decline in the mean cerebral electrical activity and, more importantly, complete loss of beta activity and marked reduction of alpha activity. There was also a pronounced increase in theta and delta activity. The reduction in beta activity was prolonged (3 minutes) and alpha activity remained abnormally low for 4 minutes.

The onset of these changes prompted a careful check of all aspects of perfusion and, when nothing abnormal was found, the surgeon was informed of the adverse CFAM changes, which were considered to represent reduced cerebral perfusion. The position of the aortic cannula was adjusted and this resulted in restoration of the voltage and frequency distribution of the CFAM trace, despite further cooling.

Postoperatively, this patient was found to have a mild left upper monoparesis which had resolved by the third day. The questionnaire at 6 weeks revealed nightmares in the second postoperative week.

Third patient

A 47-year-old man required double valve replacement for mitral and aortic valve stenosis. Six months before operation he had suffered temporary blindness in the left eye lasting 90 seconds, which was thought to be embolic in nature.

Early during CPB, at a temperature above 32°C, there was a period of hypotension; the mean arterial pressure (MAP) fell to 30 mmHg for 3–4 minutes. This was associated with an initial decline in the level of cerebral electrical activity, but then the trace became erratic and difficult to interpret for 4 minutes, before returning to a normal level. Simultaneously, the frequency analysis showed substantial slowing with complete loss of the fast (beta) activity and considerable reduction of the alpha activity, while delta and theta activity increased markedly. These changes would not normally be expected at this temperature and were related to the period of hypotension. Beta activity was lost for 4 minutes

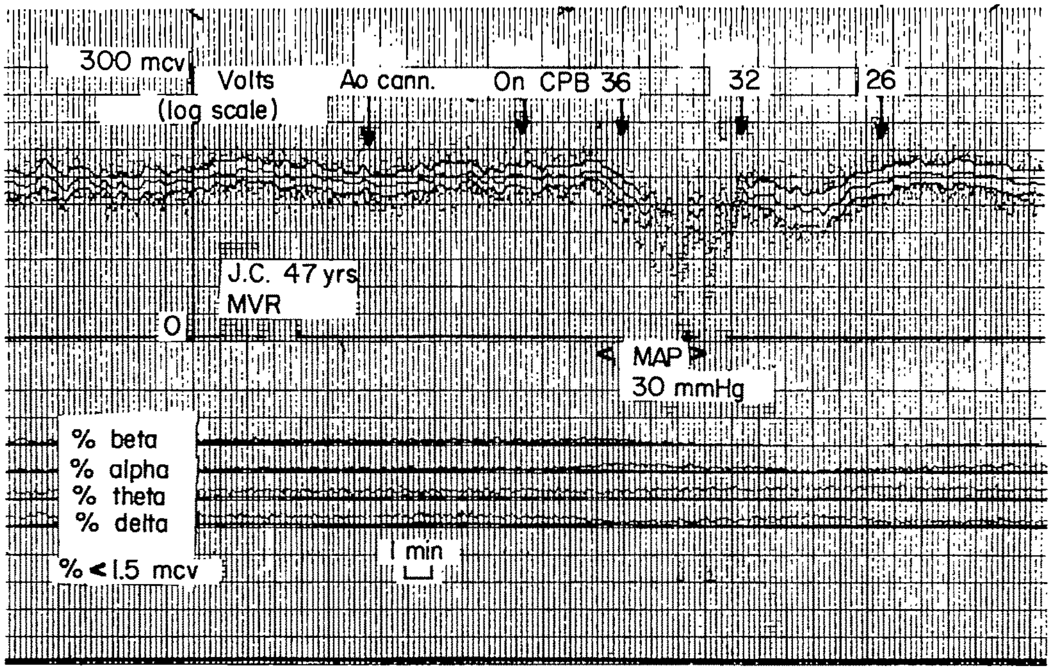


Fig. 3. The CFAM record of the third patient. Format and labelling as for Fig. 1. The trace shows a fall in voltage associated with a period of hypotension. The voltage trace becomes erratic and there is marked and prolonged loss of the faster frequencies (beta and alpha) despite restoration of the mean arterial pressure and the voltage trace.

and increased after the return of normal perfusion pressures, despite further cooling to below 26°C. Alpha activity remained considerably reduced for a longer period.

This patient suffered an extensive left hemiparesis. After a prolonged inpatient course, he was discharged home and, at that time, had considerable difficulty in walking and only slight movement of the fingers of the left hand. At 6 weeks he reported florid visual disturbances, persistent weakness of the left side, difficulty with speech and comprehension, and uncharacteristic emotional outbursts.

Fourth patient

A 63-year-old lady underwent uneventful aortic and mitral valve replacement but, before the end of CPB, at a temperature of 37°C, there was a profound fall in MAP to <25 mmHg for 1 minute, due to insufficient venous return. This produced a marked reduction in cerebral electrical activity and alteration in the frequency distribution. Beta activity ceased completely and alpha activity was greatly reduced. Delta activity was increased during the hypotensive period. When the MAP was corrected, the voltage record and frequency distributions were restored. The loss of beta activity was restored in under 2 minutes. The voltage record remained below the pre-ischaemic level for more than 5 minutes, despite a constant temperature.

Postoperatively, the patient complained only of reduced ability to concentrate, but on the 4th postoperative day she developed double vision from an internuclear ophthalmoplegia, thought to be secondary to a platelet embolus. This resolved after 48 hours treatment with dipyridamole. Follow up by questionnaire at 6 weeks revealed persistent blurring and dimming of vision, with occasional double vision, reduced concentration and some nightmares after discharge home.

Discussion

These four case histories illustrate the value of monitoring cerebral function during CPB and demonstrate clearly the importance of frequency information in the recognition of reduced cerebral perfusion from whatever cause. It is possible that cooling on CPB may have been responsible for some of the changes in voltage and frequency observed in patients 1–3. However, all changes

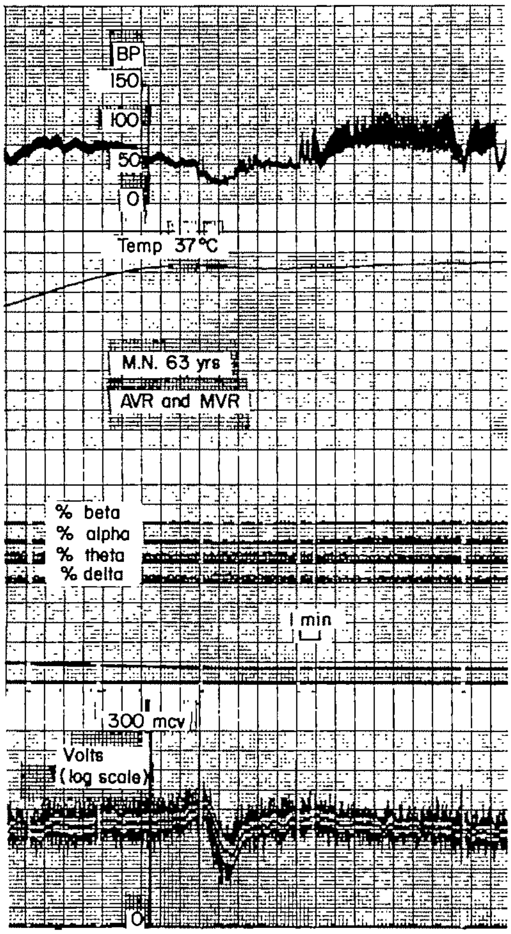


Fig. 4. The 4-channel record of the third patient showing (from above) blood pressure, temperature, frequency and analysed amplitude display. A marked fall in the mean arterial pressure is followed by a sudden deterioration of the voltage trace with a fall in the faster frequencies and an increase in the delta waveband. (Evoked potential displays occur at the five breaks in the frequency and amplitude records.)

seen developed at a nasopharyngeal temperature above 32°C, whereas previous reports of cerebral electrical activity and frequency of the EEG have described changes only at lower temperatures.[8,9] It is generally accepted that loss of fast activity (beta and alpha) is a direct result of reduced cerebral perfusion during open heart surgery.

In the first patient, the cessation of pump flow for 10 seconds had little immediate effect on the CFAM trace. This would be expected as pressure does not fall precipitously and may be below 50 mmHg for less than 5 seconds.

The presence of cerebrovascular disease can be expected to contribute to the development of cerebral ischaemia and postoperative neurological damage after CPB, but none of the patients reported here were known to suffer from carotid or vertebral arterial disease, although special investigations had not been undertaken. The presence of asymptomatic cerebrovascular disease is likely in a proportion of patients presenting for OHS, but even in those presumed to have widespread arterial disease, the value of using the CFAM is that unacceptable ischaemia in the individual patient can be detected early and accurately. The second patient also demonstrates that warning can be given to improve cerebral perfusion and minimise any cerebral damage that is occurring.

The history of the fourth patient suggests that the duration of the frequency changes produced by a fall in cerebral perfusion pressure may be indicative of the severity of the ischaemic insult, thus providing useful information for the accurate prediction of the outcome following such an event.

The third patient demonstrates that prolonged slowing of the frequency distribution of the analysed signal, is a serious prognostic sign despite a return to normal voltage. A similar pattern was seen in the first patient, where the voltage change was not marked but the frequency information was unequivocal.

The advantage of the CFAM over the conventional EEG for peri-operative monitoring is the simplicity of the display. The EEG runs at a paper speed of 30 mm/second, whereas the CFAM runs at 5 mm/minute, producing a comprehensive and easily scanned display of continuous activity and trends. Although the EEG was used in the early reports of CPB monitoring, its use was limited as it required retrospective interpretation and classification by a neurophysiologist.[8,10] Although the CFAM has the facility to produce a direct record of the EEG, this was not employed during the operative or postoperative period. A direct EEG record would have interrupted the CFAM trace. Changes in the CFAM trace are much easier to monitor for deleterious trends or improvements than the EEG. A postoperative EEG would have had little value since the changes seen on the CFAM had recovered by that stage. ●

The CFAM provides an 'on-line' analysis and a simple display, which does not require specialist interpretation, although some experience with the instrument is helpful. These are the primary requisites for new technology in this field.[6,11] The CFAM does not suffer from the disadvantages of other instruments, such as the three dimensional display and the 'blind-spots' of the Compressed Spectral Array, or the lack of precision inherent in the 'grey dots' of the Density-Modulated Spectral Array.[6,11,12]

The accuracy, simplicity and ease of interpretation of the permanent record make the CFAM a very useful instrument for monitoring patients during CPB. The first and second case histories demonstrate the early detection of minor degrees of cerebral damage and the fourth patient demonstrates that the changes can precede the development of detectable neurological damage. All the cases described illustrate the value of monitoring the frequency distribution of the analysed signal to detect the onset of impaired cerebral perfusion. The duration of the frequency changes may be of considerable importance in the prediction of the severity of the postoperative deficit.

Acknowledgments

This work was supported by a grant from the British Heart Foundation. I would also like to thank Mr M. Paneth and Dr C. Gillbe for permission to publish details of patients under their care, Dr M.A. Branthwaite for help in the preparation of the manuscript and Miss J. Mathurin for secretarial assistance.

References

1. Aberg T, Ronquist G, Tyden H, Brunkvist S, Hultman J, Bergstrom K, Lilja A. Adverse effects on the brain in cardiac operations as assessed by biochemical, psychometric, and radiologic methods. *Journal of Thoracic and Cardiovascular Surgery* 1984; **87:** 99–105.
2. Henriksen L. Evidence suggestive of diffuse brain damage following cardiac operations. *Lancet* 1984; **1:** 816–20.
3. Branthwaite MA. Detection of neurological damage during open-heart surgery. *Thorax* 1973; **28:** 464–72.
4. Prior PF. *Monitoring cerebral function: long term recordings of cerebral electrical activity.* Amsterdam: Elsevier/North Holland Biomedical Press 1979; 143–9.
5. Schwartz MS, Colvin MP, Prior PF, Strunin L, Simpson BR, Weaver EJM, Scott DF. The cerebral function monitor. Its value in predicting the neurological outcome in patients undergoing cardiopulmonary by-pass. *Anaesthesia* 1973; **28:** 611–8.
6. Levy WJ, Shapiro HM, Maruchak G, Meathe E. Automated EEG processing for intraoperative monitoring: a comparison of techniques. *Anesthesiology* 1980; **53:** 223–36.
7. Sebel PS, Maynard DE, Major E, Frank M. The cerebral function analysing monitor (CFAM). A new microprocessor-based device for the on-line analysis of the EEG and evoked potentials. *British Journal of Anaesthesia* 1983; **55:** 1265–70.
8. Peacy WC, Virtue RW. The electroencephalogram in hypothermia with circulatory arrest. *Anesthesiology* 1959; **20:** 341–7.
9. Branthwaite MA. Factors affecting cerebral activity during open-heart surgery. *Anaesthesia* 1973; **28:** 619–25.
10. Witoszka MM, Tamura H, Indeglia R, Hopkins RW, Simeone FA. Electroencephalographic changes and cerebral complications in open-heart surgery. *Journal of Thoracic and Cardiovascular Surgery* 1973; **66:** 855–64.
11. Maynard DE, Jenkinson JL. The cerebral function analysing monitor. Initial clinical experience, application and further development. *Anaesthesia* 1984; **39:** 678–90.
12. Fleming RA, Smith NT. Density modulation—a technique for the display of three-variable data in patient monitoring. *Anesthesiology* 1979; **50:** 543–6.

Anaesthesia, 1986, Volume 41, pages 67–70

CASE REPORT

Neonatal tracheal perforation

A complication of tracheal intubation

B. J. McLEOD AND E. SUMNER

Summary

Tracheal perforation following intubation in the neonatal period is rarely reported but is a serious complication that should be considered whenever difficulty in ventilation, surgical emphysema or pneumothoraces appear following intubation. Management includes the immediate and skilled replacement of the tube within the tracheal lumen and control of the air leak. Factors which increase the likelihood of occurrence of perforation are discussed.

Key words

Intubation, tracheal; complications, perforation.

Tracheal intubation of neonates is a common procedure. There is great variability in the skill of the intubator and the type of equipment available.

We report a case of tracheal perforation in a neonate by a Cole's tracheal tube used without a stylet. Tests were performed on the physical properties of these tubes, and compared with other popular neonatal tubes.

Case history

A male infant who weighed 1.6 kg was transferred to the Hospital for Sick Children, Great Ormond Street with a diagnosis of tracheo-oesophageal fistula with oesophageal atresia, left pneumothorax and hyaline membrane disease.

He had been born at 30 weeks' gestation following spontaneous rupture of membranes and vaginal delivery with Wrigley's forcep's extraction. He was apnoeic at birth and the trachea was intubated uneventfully with a 3.0-mm internal diameter Cole pattern tracheal tube (without stylet; Portex Ltd, Hythe, Kent); the lungs were ventilated for 6 minutes. He was extubated and transferred to the neonatal unit, where he again became apnoeic requiring re-intubation (2.5 mm i.d. Cole's tube without stylet). Despite ventilation, his cyanosis persisted and a left pneumothorax was found on X ray. An intercostal drain was inserted and his condition improved. Attempts to pass a nasogastric tube failed and X rays revealed it to be coiled in the upper oesophagus. His lungs were ventilated on a Bourn BP 200 Infant ventilator at a rate of 30 breaths/minute peak inspiratory pressure of 1.8 kPa with 0.5 kPa positive end expiratory pressure, and a fractional inspired oxygen concentration ($F\text{IO}_2$) 0.35. He received intravenous fluids (60 ml/kg/24 hours), penicillin and gentamicin.

B.J. McLeod, MB, ChB FFARCS, Registrar in Anaesthetics, E. Sumner, MA, BM, BCh, FFARCS, Consultant Anaesthetist, Hospital for Sick Children, Great Ormond Street, London, WC1N 3JH.

0003–2409/86/010067 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Transfer to this hospital was arranged and the results of arterial blood gas analysis at that time with $F\text{IO}_2$ 0.35 was pH 7.18; $P\text{aCO}_2$ 5.35 kPa; bicarbonate (HCO_3) 14 mmol/litre and $P\text{aO}_2$ 14.7 kPa; 3 mmol HCO_3 were given intravenously.

He was transferred by ambulance, whilst intubated and ventilated with a left chest drain, an umbilical arterial and a peripheral intravenous line *in situ*. On arrival he was cold (rectal temperature 35.1°C)) and cyanosed both centrally and peripherally. The fontanelle was flat and peripheral pulses were impalpable. There was marked bruising of the left facial and parasternal areas and swelling of the neck with crepitus. The trachea was displaced to the right and there was decreased movement of the left side of the chest with a continuous air leak into the chest drain.

He was resuscitated with plasma 30 ml/kg intravenously over 20 minutes and rewarmed. The tracheal tube was replaced uneventfully with a 2.5 mm i.d. nasal tube (Portex Ltd, Hythe, Kent) cut to a length of 9 cm and used without a stylet. Over the following hours he required increasing ventilatory pressure (3.5/0.4 kPa) and rate (45/min) to maintain acceptable gas exchange. Repeat X rays showed a small left pneumothorax, hyaline membrane disease, mediastinal and subcutaneous emphysema, gaseous distension of stomach and bowel and gas under the diaphragm.

He then underwent right thoracotomy for ligation of a tracheo-oesophageal fistula and gastrostomy. A defect was found in the trachea at the level of the fistula through which large amounts of gas leaked into the mediastinum during ventilation.

Following this there was some improvement in gas exchange, but despite this, renal function deteriorated and peritoneal dialysis was begun. Ultrasound suggested a large intraventricular haemorrhage and a computerised tomography scan confirmed this.

Brain death was diagnosed and ventilation was discontinued 8 days post delivery.

Postmortem examination of the chest revealed the sutured defect in the trachea and the ligated fistula. The trachea was otherwise grossly normal.

Discussion

Complications of tracheal intubation in children include oesophageal, pharyngeal and tracheal perforation and subglottic stenosis. Pharyngeal and oesophageal perforations occur relatively commonly following the passage of nasogastric and tracheal tubes. Subglottic stenosis is a well documented complication of longterm tracheal intubation.[1-3] In this case the perforation was associated with the use of a Cole's type of tracheal tube in a neonate with a tracheo-oesophageal fistula. These tubes are popular because of their stiffness and shouldered profile. The stiffness may make intubation easier and the shouldered profile is intended to prevent distal migration of the tube through the glottis.

We believe that these features may be associated with a greater potential for laryngeal and tracheal damage.[4] To investigate this, measurements were made of some properties of Cole's tubes and these were compared with measurements made on other popular neonatal tubes. The following measurements were made. Wall thickness (mm); this is the external diameter minus the internal diameter; tensile strength in Newtons per metre squared (N/sq m); the force required to break the tube when pulled longitudinally; elongation at breakpoint (%); the percent elongation of the tube at break point; 100% modulus (N/sq m); the force required to elongate the tube by 100 per cent when pulled longitudinally.

We compared three types of tubes, Cole's, siliconised blue line and ivory blue line (Portex Ltd, Hythe, Kent). All tests were conducted at 21°C and a relative humidity of 50%. Tests were performed in triplicate and a mean value was calculated for each size and type of tube. Standard errors have not been included.

The results (see Table 1) confirm the greater rigidity and wall thickness of Cole's tubes. The ivory tube was the least rigid in all sizes, but like the Cole's tube possessed greater wall thickness. The siliconised tube was of intermediate rigidity, but had the thinnest walls.

Excess rigidity may make perforation more likely and may, in the long term, cause glottic and subglottic damage. Greater wall thickness will increase pressure on the cricoid ring for a given internal diameter.

Putative factors increasing the incidence of perforation include rigidity of the tracheal tube, use of metal stylets, skill of the intubator, use of vigorous external laryngeal pressure during intubation, presence of anatomical abnormalities of trachea and larynx, excessive hyperextension of head and neck during intubation.

Table 1. Comparison of Cole, siliconised blue line and ivory blue line tubes

Size	Tube type	Wall thickness (mm)	Tensile strength (N/sq m × 10^6)*	100% modulus (N/sq m × 10^6)	Elongation at break points (%)
2.5 mm i.d.	Cole	0.74	29	22.8	150
	Siliconised blue line	0.50	20.2	13.3	250
	Ivory blue line	0.59	12.4	8.1	220
3.0 mm i.d.	Cole	0.72	25.9	20.6	170
	Siliconised blue line	0.56	19.0	13.8	238
	Ivory blue line	0.72	11.2	7.6	220
3.5 mm i.d.	Cole	0.67	28.2	19.6	220
	Siliconised blue line	0.65	19.5	12.7	280
	Ivory blue line	0.81	10.8	6.7	250

*N/sq m, = Newtons per square metre; i.d. internal diameter of tube.

There are four previously reported cases of tracheal perforation.[5-8] Two died immediately following the perforation[5,6] with the tips of the tracheal tubes outside the trachea in the tissues of the neck. A third case[7] also died but the report does not state whether this was a direct result of the tracheal perforation or of other disease processes.

The fourth case[8] survived tracheal perforation. Management included immediate re-intubation with a cuffed neonatal tube; the cuff apparently controlled the air leak. There was difficulty with ventilation in all four cases, and subcutaneous emphysema and pneumothoraces following intubation. None had been intubated with a Cole's tube, and three sets of authors[5,6,8] concluded that either excessive force, Magill's forceps, the nasal route or neck hyperextension was the culprit. Our case confirms that the neonatal trachea can be perforated by modern tracheal tubes even without using a stylet and consider the rigidity of the Cole's tube plus the underlying tracheal defect to be the important factors. The clinical presentation of the perforation was similar to the previously reported cases, and the subsequently successful re-intubation and control of the air leak was important for the successful initial resuscitation.

Thus, early recognition of tracheal perforation may be lifesaving. The diagnosis must be considered if difficulty with ventilation and surgical emphysema, with or without pneumothoraces, appears following intubation. If perforation has occurred, the tip of the tracheal tube may lie outside the trachea, in the tissues of the mediastinum. Withdrawal of the tube to lie within the tracheal lumen and placement of the tip below the level of the defect is advisable. If re-intubation is necessary, it may be more skilfully performed by the oral route.

If these manoeuvres fail then bronchoscopy should be considered. If mechanical ventilation is required, it should be instituted with the lowest pressures possible for acceptable gas exchange.

Large lower tracheal air leaks, as in this case, are best corrected surgically. The air leak from smaller perforations above the level of the cricoid ring may be controlled by correct positioning of a tracheal tube or tracheostomy. Broad-spectrum antibiotics are recommended in all cases to prevent mediastinitis.

Acknowledgments

The authors would like to thank Professor M. Spitz for permission to publish this case, Portex (UK) Ltd for help with measurements and Miss G. Unwin for typing the manuscript.

References

1. Othersen HB. Intubation injuries of the trachea in children. *Annals of Surgery* 1979; **189:** 601–6.
2. Johnson DE, Foker J, Munson DP, Nelson A, Athinarayan P, Thompson TR. Management of esophageal and pharyngeal perforation in the newborn infant. *Paediatrician* 1982; **70:** 592–6.
3. Fan LL, Flynn JW, Pathak DR. Risk factors

predicting laryngeal injury in intubated neonates. *Critical Care Medicine* 1983; **11:** 431–3.

4. Brandstater B. Dilatation of the larynx with Cole tubes. *Anesthesiology* 1969; **31:** 378–9.
5. Schild JP, Wuilloud A, Kollberg H, Bossi E. Tracheal perforation as a complication of nasotracheal intubation in a neonate. *Journal of Pediatrics* 1976; **88:** 631–2.
6. Serlin SP, Daily WJR. Tracheal perforation in the neonate: a complication of endotracheal intubation. *Journal of Pediatrics* 1975; **86:** 596–7.
7. Aziz EM, Suleiman KA. Tracheo-esophageal perforation in the newborn: a case report. *Clinical Pediatrics* 1983; **22:** 584.
8. Finer NN, Stewart AR, Ulan OA. Tracheal perforation in the neonate: treatment with a cuffed endotracheal tube. *Journal of Paediatrics* 1976; **89:** 510–2.

Anaesthesia, 1986, Volume 41, pages 71–72

APPARATUS

Remote monitoring using an induction loop

M. J. HARRISON AND E. J. SLATER

Summary

An electromagnetic induction loop is used to transmit signals from a pulse and respiration monitor to a standard National Health Service hearing aid to facilitate remote monitoring

Key words

Monitoring; remote.

Auditory signals have the distinct advantage that they are not directional and can therefore be recognised whether the observer is facing the monitor or not. They have the disadvantage that they are heard by all in the surrounding work area; this may not be necessary and can be very irritating.

A system has been designed that allows auditory signals to be heard by the monitoring personnel alone, up to a preset distance from the patient. The principle of inductive loop transmission is well established and these devices are in common use in schools for the deaf and in some churches and public buildings. The system comprises a hearing aid fitted with a small coil in place of its usual microphone, a facility sometimes referred to as the 'telephone' (or 'T') position. If this coil is placed within an area surrounded by a much larger coil, then a signal current in the larger coil will induce a voltage in the pickup coil. Thus, if an audio signal is used to generate the current in the transmitting coil (or loop) this will be received by the hearing aid, amplified, and reproduced in the earpiece.

Method

The indicator bulb of a conventional pulse monitor is used as the 'stimulus' for the system; its activation is detected by a photo-electric device attached to its surface. The signal from the device is used to turn an audio tone generator on and off, which, in turn, is used to drive the transmitting loop cable (Fig. 1). This tone is amplified to a preset level with an automatic gain control circuit so as to ensure a constant signal strength in the loop area. An audio power amplifier, matched to the impedance of the loop wire, is used to drive the current. The electromagnetic

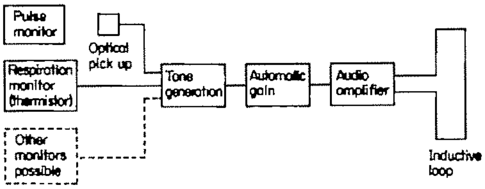


Fig. 1. Schematic diagram of complete remote monitoring system.

M.J. Harrison, MB, BS, FFARCS, Senior Lecturer and Consultant Anaesthetist, Department of Anaesthesia, Queen's Medical Centre, Clifton Boulevard, Nottingham NG7 2UH, E.J. Slater, PhD, CEng Senior Physicist (Electronics), Department of Medical Physics, City Hospital, Hucknall Road, Nottingham NG5 1PB.

0003–2409/86/010071 + 02 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

field variation set up by this current is detected by a conventional National Health Service hearing aid with the input switch turned to the 'telephone' ('T') position. The pulse signal is used to turn on a 1 kHz tone generator, which mimics the actual audio output from the pulse monitor. This tone burst lasts about 0.5 seconds.

Representing respiration is more difficult, as there is no generally accepted audio system in use. We have used a lower frequency tone (*c.* 300 Hz, duration 1 second) to signify inhalation. This provides a sufficiently different sound that simultaneous monitoring of pulse and respiration is quite simple. Detection of respiration is achieved by inserting a thermistor into the breathing system, near to the patient's mouth.

Discussion

The system was found to work satisfactorily when the area over which the signals were required to be heard (Fig. 2) was covered by multiple loops of the induction coil installed in the theatre roof space. This produced a signal level that was more consistent and therefore reduced the necessity for continual alteration of amplification at the receiving end. Signal strength rapidly declined when moving out of the area covered by the loop; this allows the system to be used in two adjacent theatres, since interference is virtually eliminated.

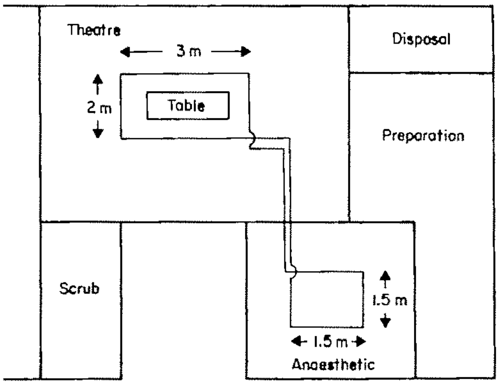


Fig. 2. Layout of induction loop in theatre roof space.

The power of the transmitted field in this type of system is restricted by Home Office regulations in the United Kingdom; however, the level of signal used is well below the permitted maximum. Because of the nature of the signal and its low power there is no danger of interference to or from other monitoring systems. Although interaction is possible between two adjacent loops, of the type described here, careful loop layout and power-setting reduces this to a negligible amount.

The major criticism of this system is that it would enable patient monitoring from the 'coffee room'. This is not a practice to be encouraged and can be overcome by correct configuration of the loop and by presetting the power from the loop amplifier. However, the system does allow for continued monitoring during routine procedures such as preparing drugs in the nearby anaesthetic room, and whilst talking to other staff, away from the 'console' area of the anaesthetic machine. Normal conversation can take place whilst listening to the monitors, since the ear piece is designed to fit comfortably around the pinna of the ear and is not inserted into the external auditory canal. Those individuals who desire continuous cardiovascular and respiratory monitoring will welcome the device, as it enables more freedom of movement within the operating theatre and anaesthetic room.

There is, as yet, no standard for auditory warnings in intensive care wards or operating theatres, but there is a British Standards Institution working party on this task. Much work has already been documented on the ability of flight crews to hear, recognise and act, in a controlled yet appropriately urgent manner, to alarms from many sources. Some of the recommendations laid down by Patterson[1] are that auditory warning sounds should be at least 15 dB above the threshold level of the background noise, that there should be no more than six immediate-action warning sounds and three attensons (i.e. attention demanding sounds) and that voice warnings should be brief and use a key word format.

The system described is, strictly speaking, not an auditory warning system but an auditory monitoring system. However, these recommendations are useful in that further development of this monitoring process could well incorporate warnings, either vocal or simple alarms, and the general principles regarding noise levels and the number of signals must then be relevant. The role of the voice in such warnings is to eliminate the possibility of confusion. Obviously, this is not a problem with only two signals, at frequencies of 1 kHz and 300 Hz.

Reference

1. Patterson RD. Guidelines for auditory warning systems on civil aircraft. Civil Aviation Authority Paper 82017, 1982.

Anaesthesia, 1986, Volume 41, pages 73–76

Forum

Cryoanalgesia for pain after herniorrhaphy

R.C. Khiroya, MB, BS, FFARCS, Senior Registrar, Department of Anaesthetics, Charing Cross Hospital, Fulham Palace Road, London W6 8RF, H.T. Davenport, MB, FRCP(C), FFARCS, Consultant Anaesthetist and J.G. Jones, MD, FFARCS, FRCP, Scientific Staff, MRC, and Hon. Consultant Anaesthetist, Clinical Research Centre and Northwick Park Hospital, Watford Road, Harrow, Middlesex, HA1 3UJ.

Summary

The effect of freezing the ilioinguinal nerve on postoperative pain relief was examined in a double blind study in 36 patients undergoing herniorrhaphy, randomly allocated into two groups. Patients in the experimental group had their ilioinguinal nerves frozen during surgery and were compared with the patients in the control group who did not have cryoanalgesia. Pain relief was assessed overa 48-hour period in three ways, namely the linear analogue pain scale, peak expiratory flow rates and the amount of analgesic drugs required by patients in the two groups. We conclude that cryoanalgesia of the ilioinguinal nerve alone does not produce significant early post herniorrhaphy pain relief.

Key words

Pain; postoperative.
Equipment; cryoprobe.

Freezing of the ilioinguinal nerve during surgery has been described as a satisfactory method for relieving the pain after herniorrhaphy.[1] It is said to be a particularly suitable technique for day care patients as they needed less analgesic drugs and resumed normal activity earlier. When a herniorrhaphy is done under local analgesia three nerves must be blocked;[2] these are the iliohypogastric, ilioinguinal and the genitofemoral nerves. In view of the claim that cryoanalgesia of the ilioinguinal nerve alone is a satisfactory technique, this study was undertaken to see if freezing a single nerve was, in fact, a satisfactory method of postherniorrhaphy pain relief.

Method

The trial was approved by Northwick Park Hospital Ethical Committee. All patients studied gave informed consent. Patients who were admitted for inguinal hernia repair (36 males) took part in the study. The mean age of patients in the cryoanalgesia group was 50.8 years with a range of 30–74 years and the mean age of the control group was 50.6 years with a range of 36–66 years. The patients were assessed for cardiovascular, respiratory, metabolic and central nervous system abnormalities. All patients fulfilled the criteria of ASA Class I or II. They were randomly allocated to two groups, the experimental and the control. The patient and the observer did not know to which group the patient belonged. Pre-operative peak expiratory flow was measured using a Wright's Mini Peak Flow Meter. No pre- or intra-operative analgesics or local anaesthetics were used in order to avoid confusing the assessment of cryoanalgesia in the immediate postoperative period.

Anaesthesia was induced with sodium thiopentone and maintained with oxygen, nitrous oxide and halothane using a mask and Guedel airway. None of these agents have any lasting analgesic effects.[3,4]

Hernia repair was carried out in a standard manner. At the end of operation, before skin closure, the patients in the experimental group had the ilioinguinal nerve blocked as follows. The nerve was lifted and hooked by the surgeon onto the previously sterilised cryoprobe.

Correspondence should be addressed to: Dr R.C. Khiroya, Department of Anaesthetics, Charing Cross Hospital, Fulham Palace Road, London W6 8RF.

0003–2409/86/010073 + 07 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

No extra dissection was necessary to expose the nerve. The nerve was frozen for two periods of one minute each, with an interval of 30 seconds in between to allow thawing.

In the recovery ward, when the patient was able to cooperate, his pain was scored on the visual linear analogue scale which is simple and easy to use.[5] Peak expiratory flow rate was also measured at this time. These measurements were repeated 4 hours and 8 hours later on the day of the operation and on the first and second postoperative days.

All the patients who complained of pain were given analgesic drugs. These were an injection of pethidine if the pain was severe and Distalgesic tablets if it was moderate. A record was kept of all analgesic drugs administered.

Results

The mean pain scores in the experimental (cryo-analgesia) and control groups are shown in Fig. 1. The maximum pain scores were observed within the first 4 hours of the operation. Statistically, the difference between the two groups was not significant. On the second day, the experimental group seemed to have had a tendency to less pain, but this difference was again not statistically significant.

The mean reduction in peak expiratory flow (PEF) from the pre-operative value is shown in Fig. 2 at different time intervals following surgery. Both groups showed a similar pattern of response. Although the mean PEF was greater in the experimental group, the difference was not statistically different in the treated and untreated groups at any time.

The mean number of doses of pethidine and Distalgesics for the control group was 1.0 and 3.8 respectively and that for the experimental group was 1.1 and 3.7 respectively. The amount of pethidine and Distalgesic tablets that were required by the patients in the two groups is shown in Fig. 3. Again, the difference between the two groups was not statistically significant.

Discussion

Freezing a nerve, as described in this study, produces a reversible nerve lesion of the second degree, according to Sunderland's classification.[6] Absence of damage to the nerve and minimal inflammation ensures that regeneration of function is complete and occurs at the rate of about 1–33 mm per day.[7,8] In theory, therefore, it seems to be a suitable technique for postoperative pain relief for any operation when a sensory nerve is easily accessible, and freezing intercostal nerves has been shown to reduce the need for analgesic drugs after thoracotomy.[9] The ilioinguinal nerve is a readily accessible nerve which is distributed to the skin over the root of the penis and upper part of the scrotum in the male and to the skin covering the mons pubis and the adjoining part of the labium majus in the female.[10] The incision for inguinal hernia repair is usually made 1 cm above and parallel to the inguinal ligament. This area is not supplied by the ilioinguinal nerve and freezing this nerve alone will have limited effect on postoperative pain.

In our study, no pre- or intra-operative analgesia was used. All our patients had the same anaesthetic agents and technique and pain was assessed using three different methods: resting pain measured with the linear analogue scale, a graded painful stimulus and patient requirement for analgesic drug. None of these methods showed any significant improvement in postoperative analgesia in the cryoanalgesia group.

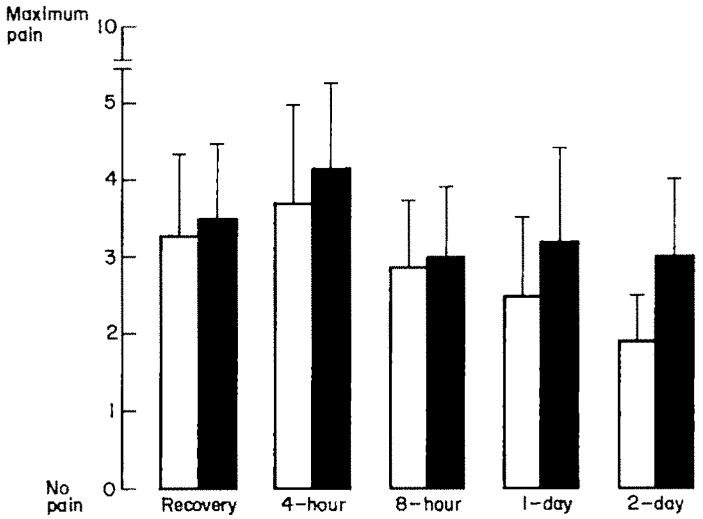


Fig. 1. Histogram of pain scores. The bars represent SE of the mean. □, experimental; ■, control.

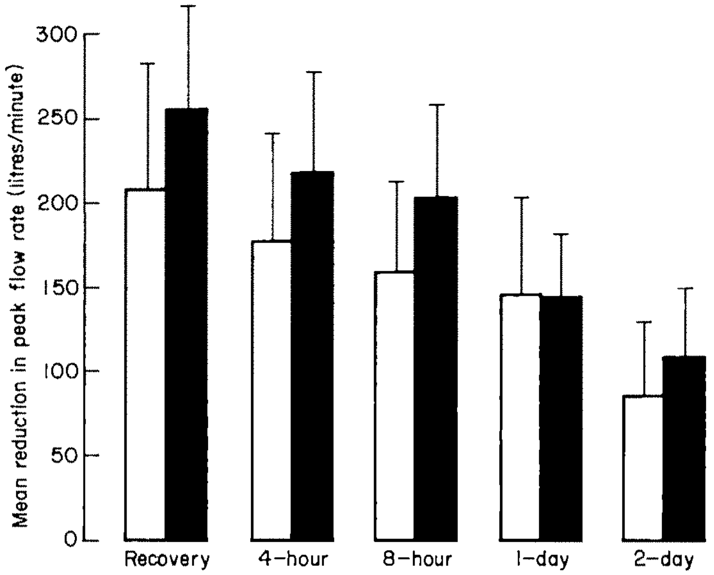


Fig. 2. Histogram of mean reduction in peak flow rate. The bars represent SE of the mean. □, experimental; ■, control.

Wood *et al.*[1] concluded that cryoanalgesia of the ilioinguinal nerve appeared 'to be a significant advance in postoperative analgesia both for inpatient and for day care or short stay patients'. Their use of epidural analgesia, using either lignocaine or bupivacaine may have influenced their results. Both local anaesthetic agents have varying duration of action ranging from 1–6 hours;[12] this effect could have reduced the need for analgesia in some of their patients.

We used peak expiratory flow as an index of pain relief for the following reasons. It has previously been shown[12] that vital capacity (VC), forced expiratory volume in one second (FEV_1) and PEF are all reduced to below 80% of the pre-operative value following abdominal surgery. This is presumably due to the pain associated with the contraction of chest wall (rib cage/diaphragm/abdomen) musculature. Each of these manoeuvres requires different amounts of muscle contraction. For example, the pressure required to achieve a maximal value of $FEV_{1.0}$ is about 2.5 kPa, the vital capacity effort ranges from 2.5 to −2.5 kPa but the PEF effort may exceed 12.0 kPa.[13] There is also a very non-linear relationship between pressure (i.e. effort) and FEV_1 and VC, whereas the relationship between effort and PEF is such that this test gives much more information about graded expiratory effort overa very large range of flows. Because of the greater muscle contraction in PEF, it is not surprising that little improvement in PEF is seen after papaveretum[12] and that there is a smaller improvement in PEF than with VC after nitrous oxide and morphine.[14]

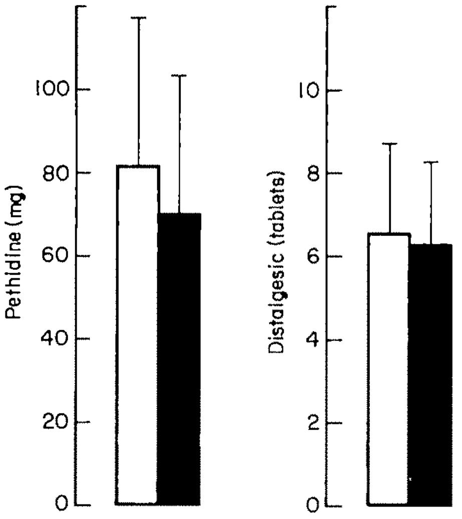


Fig. 3. Histogram of pethidine and Distalgesics required by the two groups. The bars represent SE of the mean. □, experimental; ■, control.

This study showed that in the 48-hour period following surgery, cryoanalgesia to the ilioinguinal nerve alone did not reduce the pain experienced by the patients following a hernia repair, neither did it reduce the analgesic requirement. This result contrasts with that of Wood *et al.*, who used day care patients, epidural anaesthesia and a longer follow-up.

Acknowledgments

We would like to thank Mr A.G. Cox, MD, FRCS for allowing us to carry out this study on his patients. We thank the nursing staff for their cooperation and Mr Charles Rossiter of the Department of Computing and Statistics for his advice. We also thank Brenda Dobson and Norma Saunders for secretarial help.

References

1. Wood GJ, Lloyd JW, Bullingham BJ, Finch DRA. Postoperative analgesia for day-case herniorrhaphy patients. A comparison of cryoanalgesia, paravertebral blockade and oral analgesia. *Anaesthesia* 1981; **36:** 603–10.
2. Erickson E. *Illustrated handbook in local anaesthesia.* London: Lloyd-Luke (Medical Books) Ltd, 1979.
3. Dundee JW. Thiobarbiturates. In: Feldman SA, Scurr CF. eds. *Intravenous anaesthetic agents. Current topics in anesthesia series.* 1979: 8–9.
4. Henderson JJ, Parbrook GD. Influence of anaesthetic technique on postoperative pain. A comparison of anaesthetic supplementation with halothane and with phenoperidine. *British Journal of Anaesthesia* 1976; **48:** 587–92.
5. Rosen M. The measurement of pain. In: Harcus AW, Smith R, Whittle B, eds. *New perspective in pain measurement* Edinburgh: Churchill-Livingstone, 1977: 14–5.
6. Sunderland S. A classification of peripheral nerve injuries producing loss of function. *Brain* 1951; **74:** 491–516.
7. Beazley RM, Bagley DH, Ketcham AS. The effect of cryosurgery on peripheral nerves. *Journal of Surgical Research* 1974; **16:** 231–4.
8. Evans PJD. Cryoanalgesia. The application of low temperatures to nerves to produce anaesthesia or analgesia. *Anaesthesia* 1981; **36:** 1003–13.
9. Katz J, Nelson W, Forest R, Bruce DL. Cryoanalgesia for post-thoracotomy pain. *Lancet* 1980; **1:** 512–3.
10. Warwick R, Williams P. eds. *Gray's Anatomy*, 35th ed. London: Longman 1973: 105.
11. Bromage PR, Gertel M. An evaluation of two new local anaesthetics for major conduction blockade. *Canadian Anaesthetists' Society Journal* 1970; **17:** 557–64.
12. Masson AHB. Clinical assessment of analgesic drugs: spirometry trial. *Anesthesia and Analgesia* 1962; **41:** 615–22.
13. Zamel N, Jones JG, Bach SM, Newberg L. Analog computation of alveolar pressure and airway resistance during maximum expiratory flow. *Journal of Applied Physiology* 1974; **36:** 240–5.
14. Parbrook GD, Rees GAD, Robertson GS. Relief of postoperative pain: comparison of a 25% nitrous-oxide and oxygen mixture with morphine. *British Medical Journal* 1964; **2:** 480–2.

Anaesthesia, 1986, Volume 46, pages 77–79

Epidural buprenorphine for postoperative analgesia. A controlled comparison with epidural morphine.

J. Wolff, MD, Registrar, P. Carl, MD, Senior Registrar, M.E. Crawford, MD, Senior Registrar,
Department of Anaesthesia, Esbjerg Central Hospital, 6700 Esbjerg, Denmark.

Summary

In a double-blind controlled study, epidural buprenorphine 0.3 mg was compared with 4 mg of epidural morphine for postoperative pain relief the first 24 hours after major orthopaedic surgery. The degree of analgesia was equal and satisfactory in both groups. Duration of action was 620 minutes with buprenorphine and 580 minutes with morphine, which was not significantly different. The only serious side effects were recorded in the morphine group, with two patients complaining of pruritus and five of urinary retention. In conclusion, epidural buprenorphine did not offer any advantages in preference to morphine for postoperative pain relief following orthopaedic surgery.

Key words

Anaesthetic techniques, regional; epidural.
Analgesics, narcotic; morphine, buprenorphine.

The demonstration of specific opiate receptors in the substantia gelatinosa of the spinal cord[1] and the subsequent original clinical application,[2] resulted in a widespread use of epidural opiates in the treatment of chronic and postoperative pain. Although most clinical reports deal with the use of epidural morphine chloride, other opioids have been investigated.[3]

Buprenorphine is a relatively new synthetic opioid, with both agonistic and antagonistic properties; high receptor affinity and great lipid solubility have been

---

Correspondence should be addressed to Dr J. Wolff, Department of Anaesthesia, Bispebjerg Hospital, Bispebjerg Bakke 23, 2400 Copenhagen NV, Denmark.

demonstrated.[4] The present study was undertaken to compare the analgesic properties and side effects of epidural buprenorphine and morphine in the treatment of postoperative pain after orthopaedic surgery on the lower extremities. In every case, the morphine used was in the form of the hydrochloride.

Methods

Forty patients of ASA grades 1 or 2 and undergoing internal fixation of fractures of the lower limbs were allocated randomly to one of two groups. All patients gave their informed consent pre-operatively and the trial was conducted in accordance with the Helsinki II Declaration. Patients with chronic consumption of analgesics, who were uncooperative or in whom an epidural was contraindicated, were not included in the study.

Both groups were premedicated with oral flunitrazepam 1 mg, one hour pre-operatively. Anaesthesia was induced with flunitrazepam and maintained with nitrous oxide/oxygen, fentanyl and pancuronium. Immediately after termination of the operation, a lumbar epidural catheter was inserted at the level of L_{2-3} and advanced 5 cm into the epidural space in a cephalad direction.

In the recovery room, when analgesia was requested by the patient, either 4 mg morphine diluted to 10 ml with normal saline ($n = 20$), or 0.3 mg buprenorphine in the same dilution ($n = 20$) was injected through the epidural catheter. When further analgesia was demanded during the next 24 hours, the same dose was administered epidurally. Neither the patients nor the observer were aware of which opiate was being given and no other analgesics were administered during the postoperative period.

Pain intensity was assessed by the patient on a 0–4 rank scale (0 = no pain; 1 = mild pain; 2 = moderate pain; 3 = severe pain; 4 = intolerable pain) before, and 10, 20, 30 and 60 minutes, after each injection and then every 180 minutes or until a further dose was given. The reduction in pain score at each observation time after injection was calculated as the pain intensity difference (PID). The sum of pain intensity difference scores (SPID) was calculated by adding the product of each post-administration PID and the corresponding time interval since the previous observation.

Arterial blood pressure, heart rate and respiratory rate were measured before and 5, 15 and 30 minutes after each injection and then every hour during the study. Motor function and sensation to touch and pinprick were evaluated before and 30 minutes after the epidural injection. All subjective and objective side effects were registered. All observations were made by the same physician.

Fisher's test was used for statistical analysis of unwanted side effects and Mann Whitney unpaired rank sum test was used for all other data. Significance was assigned at a level of 0.05.

Results

Demographic data and total consumption of anaesthetic and muscle relaxant agents preoperatively are shown in Table 1. There were no statistically significant differences between the groups. The median number of injections during the first 24 postoperative hours for both groups was 2.0, corresponding to a total median consumption of 8 mg morphine and 0.6 mg buprenorphine (Table 2). Duration of analgesia was 580 minutes in the morphine group and 620 minutes following buprenorphine; this difference was not significant. Reduction in pain intensity (PID) after 30 minutes and SPID are shown in Table 3. No patients required additional systemic analgesia.

No loss of motor function or sensation was found in either group. Only minor changes in blood pressure, heart rate and respiratory rate were observed. There were no instances of respiratory depression. The unwanted side effects are shown in Table 4, and were more frequent in the morphine group, although the difference was not statistically significant. Pruritus and urinary retention were not observed following buprenorphine.

Table 1. Demographic data and total consumption of anaesthetic and muscle relaxant agents. Median (range)

	Morphine chloride	Buprenorphine	p
Sex	10 M, 10 F	10 M, 10 F	NS
Age (years)	61 (20–69)	60 (16–69)	NS
Total dose of flunitrazepam (mg)	0.9 (0.4–1.8)	1.0 (0.4–2.8)	NS
Total dose of fentanyl (mg)	0.35 (0.20–0.80)	0.40 (0.20–0.80)	NS
Total dose of pancuronium (mg)	9.0 (4–19)	9.0 (4–14)	NS

Table 2. Number of injections during the first 24 hours postoperatively and total consumption of opiate. Median (range)

	Morphine chloride	Buprenorphine	p
Number of injections	2.0 (1–5)	2.0 (1–6)	NS
Total dose of opioid (mg)	8.0 (4–20)	0.60 (0.3–1.8)	

Table 3. Duration of analgesia, pain intensity difference scores (PID), and the sum of pain intensity difference scores (SPID). Median (range)

	Morphine chloride	Buprenorphine	p
Duration of analgesia (minutes)	580 (30–1440)	620 (30–1440)	NS
PID	1.90 (0.0–4.0)	2.0 (0.0–4.0)	NS
SPID	2.60 (0.16–9.0)	3.30 (0.16–12.0)	NS

Table 4. Number of patients with unwanted side effects

	Morphine chloride	Buprenorphine
Headache	1	0
Nausea	4	3
Vomiting	1	2
Pruritus	2	0
Urinary retention	5	0
Mental confusion	1	1
Dizziness	2	2
Drowsiness	4	4

There were no other serious side effects requiring treatment.

Discussion

Systemic buprenorphine provides postoperative analgesia of long duration with only minor unwanted side effects.[5,6] With an assumption of certain theoretical advantages, including high receptor affinity and high lipid solubility, Rondomanska *et al.*,[7] in an open trial, showed that epidural administration of 0.3 mg buprenorphine was safe and effective for postoperative pain relief. The duration of action was in excess of 24 hours in over half of the patients. Other investigations have demonstrated prolonged pre-operative and postoperative analgesia using buprenorphine 0.3 mg as an analgesic supplement to bupivacaine.[8] In the present study, a dose of 0.3 mg buprenorphine was compared with 4 mg morphine for postoperative pain relief, to confirm the results mentioned above, but in a controlled manner. Furthermore, our previous clinical experience with long term treatment of chronic pain with epidural opiates has shown that a relatively high dose of buprenorphine was required to obtain sufficient analgesia.

Our results demonstrated that the quality of analgesia was equal and satisfactory in both groups. The median duration of action of buprenorphine was slightly longer than that of morphine but the duration of analgesia was only somewhat longer than following its parenteral administration. We suspect that systemic absorption is therefore the main mode of action. This, in fact, may be explained by the high lipid solubility and molecular weight of buprenorphine, leading to rapid vascular removal and also its low dural permeability, as suggested by *in vitro* experiments.[9]

Long duration of pain relief achieved with even smaller doses of epidural buprenorphine have been reported from other sources.[10] However Lanz *et al.*,[11] in their investigation, did not find that epidural buprenorphine in a dose of 0.15 mg was sufficient for postoperative analgesia following orthopaedic surgery. On the other hand, with a dose of 0.3 mg, pain relief for about 12 hours was achieved. In that study, postoperative analgesia was achieved with epidural mepivacaine or bupivacaine and potentiation by these drugs could not be excluded. A somewhat shorter duration of analgesia with 0.15 mg buprenorphine was found in another comparative study.[12]

Unwanted side effects were more frequent in the morphine group, where two cases of pruritus and five of urinary retention were recorded. These side effects have also frequently been described in other studies[13-15] and may be explained by the physicochemical properties of buprenorphine. Early or late respiratory depression was not observed in any group. In this respect, epidural buprenorphine may possess a theoretical advantage compared to morphine, due to its high lipid solubility.[16]

In conclusion, 0.3 mg buprenorphine administered epidurally provided similar analgesic properties when compared to 4 mg morphine, and did not offer any advantages over morphine for postoperative pain relief following orthopaedic surgery.

References

1. Pert CB, Snyder SH. Opiate receptor: demonstration in nervous tissue. *Science* 1973; **179**: 1011–4.
2. Behar M, Magora F, Olshwang D, Davidson JT. Epidural morphine in treatment of pain. *Lancet* 1979; **1**: 527–9.
3. Bromage PR, Camporesi E, Chestnut D. Epidural narcotics for postoperative analgesia. *Anesthesia and Analgesia* 1980; **59**: 473–80.
4. Hambrook JM, Rance MI. The interaction of buprenorphine with the opiate receptor. Lipophilicity as a determining factor in drug-receptor kinetics. In: Kosterlitz HW, ed. *Opiates and endogenous opioid peptides*. Amsterdam: Elsevier North-Holland, Biomedical Press, 1976: 295–301.
5. Harcus AH, Ward AE, Smith DW. Buprenorphine in postoperative pain results in 7500 patients. *Anaesthesia* 1980; **35**: 382–6.
6. Kay B. A double-blind comparison of morphine and buprenorphine in prevention of pain after operation. *British Journal of Anaesthesia* 1978; **50**: 605–9.
7. Rondomanska M, De Castro J, Lecron L. The use of epidural buprenorphine for the treatment of postoperative pain. In: Yaksh T, Müller H, eds. *Spinal opiate analgesia. Experimental and clinical studies. Anaesthesiology and Intensive Care Medicine*. Springer Verlag, 1982; **144**: 91–4.
8. Louis C, Freye E, Hartung E, Haag W. Buprenorphin in der periduralen Leitungsanasthesie. *Anästhesia und Intensiv Notfallmedizine* 1981: **17**: 341–4.
9. Moore RA, Bullingham RES, McQuay HJ, Hand .CW, Aspel JB, Allen MC, Thomas D. Dural permeability to narcotics: *in vitro* determination and application to extradural administration. *British Journal of Anaesthesia* 1982; **54**: 1117–28.
10. Cahill J, Murphy D, O'Brian D, Mulhall J, Fitzpatrick G. Epidural buprenorphine for pain relief after major abdominal surgery. *Anaesthesia* 1983; **38**: 760–4.
11. Lanz E, Simko G, Theiss D, Glocke MH. Epidural buprenorphine. A double-blind study of postoperative analgesia and side effects. *Anaesthesia and Analgesia* 1984; **63**: 593–8.
12. Zenz M, Piepenbrock S, Hübner B, Glocke M.

Periduralen Analgesie mit Buprenorphin und Morphin bei postoperativen Schmerzen. *Anästhesie und Intensiv Notfallmedizine* 1981; **16**: 333–9.

13. Reiz S, Westberg M. Side effects of epidural morphine. *Lancet* 1980; **2**: 203–4.
14. Gustafsson LL, Schildt B, Jacobsen K. Adverse effects of extradural and intrathecal opiates: report of a nationwide survey in Sweden. *British Journal of Anaesthesia* 1982; **54**: 479–86.
15. Bromage PR, Camporesi EM, Durant PAC, Nielsen Rostral spread of epidural morphine. *Anesthesiology* 1982; **56**: 431–6.
16. Bromage PR. The price of intraspinal narcotic analgesia: basic constraints. *Anesthesia and Analgesia* 1981; **60**: 461–3.

Anaesthesia, 1986, Volume 41, pages 80–93

Correspondence

Prognosis in shock 80
M.H. Weil, MD, PhD. J. Leavy and E.C. Rackow, MD
I. McA. Ledingham, MD, FRCSE, MRCP, FRSE 81
Safe obstetric anaesthesia—just an ideal 82
C. Ramamoorthy, FFARCS
Abortions among dental personnel exposed to nitrous oxide 82
H.C. Schuyt, K. Brakel, MD, S.G.L.M. Oostendorp, BSc and B.J.M. Schiphorst
Oxygen concentrators 83
D. Lush, FFARCS
Atracurium and vecuronium in emergency eye surgery 84
S. Mallaiah, FFARCS, R.J. Eltringham, FFARCS and D.M. Magauran, FRCS
Susceptibility to malignant hyperpyrexia 85
F.R. Ellis, PhD, FFARCS and P. Jane Halsall, MB, ChB
M.A. Moxon, FFARCS 86
Tracheal tube obstruction by prominent aortic knuckle 86
J. Martin, FFARCS and B. Hutchison, FFARCS
Local analgesic convulsions and epidural analgesia for Caesarean section 87
L.E.S. Carrie, FFARCS
C.M. Wilson, FFARCS and J. Moore, MD, PhD, FFARCS 88
An alternative to Allen's test 88
P.W. Duncan, FFARCS
Petechial rashes and automatic blood pressure measurement 88
B.J. Nicholls, FFARCS and D.W. Ryan, FFARCS
Epidural meptazinol 88
R.I. Francis, FFARCS and A.S. Lockhart, FFARCS
Non vagolytic anaesthetic sequence—sinus arrest 89
M. Higgins, MB, ChB, BSc, and J.M. Thorp, MRCP, FFARCS
More on combined subarachnoid and epidural techniques 90
C.M. Kumar, DTCD, FFARCS
Accidental disconnexion following inactivation of Servoventilator alarm 91
M.R.J. Sury, FFARCS, C.J. Hinds, MRCP, FFARCS and M. Boustred
Tonsillar enlargement and palatal surgery 91
B.C. Sellick, FFARCS
Anaesthesia in myopathy of carnitine deficiency 92
B. Beilin, MD, D. Shulman, BSc, MD, and Y. Schiffman, MD
Atracurium and McArdle's disease 93
A. Rajah, MB, ChB, and Christine F. Bell, FFARCS
Difficult tracheal intubation 93
W.F.S. Sellers, FFARCS, and G.W. Jones, BSc, MRCP, FFARCS
Recovery? 93
J.M. Cundy, FFARCS

Prognosis in shock

The study by Dr Cowan (*Anaesthesia* 1984; **39**: 750–5) is of substantial interest. However, the conclusion that lactic acid has little prognostic value in the prediction of outcome is an artifact of the statistical treatment applied to their data and is at variance with firmly supported scientific opinion that lactic acid does indeed indicate severity and predict outcome.[1–7]

The authors conclude, through the use of dis-

All correspondence should be addressed to Dr J.N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

Letters must be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters contained in 'Notice to Contributors' to *Anaesthesia* printed at the back of each issue. The degrees and diplomas of each author must be given in a covering letter personally signed by all the authors.

Correspondence presented in any other style or format may be the subject of considerable delay and may be returned to the author for revision.

criminant analysis, that absolute values of lactate and serial measurements of lactate contribute little to the prediction of outcome. Lactic acid was a weak discriminator when analysed in conjunction with urine output, peripheral temperature gradients and changes in arterial pressures. This does not, however, mean that lactic acid by itself is not a statistically significant variable when used to discriminate outcome as a single parameter.

In the data reported by Cowan, whole blood lactate declined within 3 hours and continued to decline over an interval of 24 hours in survivors. These reductions were significant at the $p<0.01$ level. In contrast, fatal cases had either no reduction of lactate or an increase in whole blood lactate concentrations between 3 and 24 hours. These changes paralleled those in mean arterial pressure and core–peripheral temperature gradients. Urine volumes, however, were significantly increased at 3 hours in both the survivors and the non-survivors, thereby decreasing the apparent specificity of this measure.

There are two additional considerations that should be addressed in the interpretation of the data. The very high lactates, referred to as 'outliers' by the authors, may well have reflected transient lactate increases related to chills and physical exertion of patients during sepsis. These artefacts of lactate measurement are well recognised and can be clinically identified. Moreover, the fact that oxygen consumption may be normal or even increased during sepsis does not necessarily support the assumption of the authors that this would militate against anaerobic metabolism. Oxygen consumption is markedly increased during stress. The issue is whether oxygen delivery fulfills the aerobic requirements of the patient. In the case of maximal exercise of short duration, marked lactic acidosis is in evidence because extreme increases in oxygen consumption still do not fulfill tissue requirements for oxygen.[8]

Finally, the authors cite two publications in support of their conclusion that lactic acid fails as a competent predictor of outcome.[9,10] In the first, Cerra *et al.*[9] reported that with lactate increases in the range of 2 mmol/litre or less, measurement of pyruvate and the calculation of the lactate/pyruvate ratio is of value. However, even in this study changes in blood lactate concentrations accurately reflected eventual outcome in patients with septicaemia. Perret and Enrico[10] do not invalidate lactic acid for estimating prognosis, but point to the disproportionately high lactate levels that are observed in patients with severe hepatic dysfunction.

Accordingly, the statement that lactate is useless as a predictor of outcome is not appropriately supported by this isolated report.

University of Health Sciences
The Chicago Medical School,
3333 Green Bay Road,
North Chicago, Illinois 60064
USA

M.H. Weil
J. Leavy
E.C. Rackow

References

1. Broder G, Weil MH. Excess lactate: an index of reversibility of shock in human patients. *Science* 1964; **143**: 1457–9.
2. Peretz DI, McGregor M, Dossetor JB. Lacticacidosis: a clinically significant aspect of shock. *Canadian Medical Association Journal* 1964; **90**: 673–75.
3. Weil MH, Afifi AA. Experimental and clinical studies on lactate and pyruvate as indicators of the severity of acute circulatory failure (shock). *Circulation* 1970; **41**: 989–1001.
4. Vitek V, Cowley RA. Blood lactate in the prognosis of various forms of shock. *Annals of Surgery* 1971; **173**: 308–13.
5. Cady LD, Weil MH, Afifi AA, Michaels SF, Liu UY, Shubin H. Quantitation of severity of critical illness with special reference to blood lactate. *Critical Care Medicine* 1973; **1**: 75–80.
6. Henning RJ, Weil MH, Weiner F. Blood lactate as prognostic indicator of survival in patients with acute myocardial infarction. *Circulatory Shock* 1982; **9**: 307–15.
7. Vincent JL, DuFaye P, Berre J, Leeman M, Degaute JP, Kahn RJ. Serial lactate determinations during circulatory shock. *Critical Care Medicine* 1983; **11**: 449–51.
8. Astrand PO, Rodahl K. *Textbook of work physiology.* New York: McGraw Hill Book Company, 1977: 291–8.
9. Cerra FB, Wiles CE, Barder JR, Siegel JH, McMenamy RH. You need to know more than lactate in sepsis. *Critical Care Medicine* 1981; **9**: 236.
10. Perret C, Enrico JF. Lactate in acute circulatory failure. In: Bossart H, Perret C, Eds, *Lactate in acute conditions.* Basel: Karger, 1979: 69–82.

A reply

This is a somewhat belated (for which I apologise) reply to the observations made by Dr Weil and his colleagues concerning our study published last year.

The first point concerns 'the artifact of statistical treatment'. Discriminant analysis, as used in this study, is an appropriate technique for comparison of the *relative* importance of individual variables. The central observation of this study was that, of the four variables measured (three of which were routine haemodynamic values), lactate proved to be the least important; that observation remains secure and unchallenged. We accept that this does not mean that lactate when used as a single parameter is not a statistically significant variable. Indeed, we showed that this was the case.

We note the speculation of Dr Weil and his colleagues concerning the aetiology of the occasional very high lactate values, but would point out that these occurred in both survivors and non-survivors; physical exertion was not observed in our sedated, ventilated patients! We doubt the relevance of the analogy between short duration, maximal exercise to the complex metabolic disturbance of sepsis where abnormalities of lactate clearance, not necessarily related to hypoxia, undoubtedly influence blood lactate levels.

Finally, the main burden of the two supporting publications cited by us was that, in certain common clinical situations, interpretation of the prognostic significance of lactate is difficult.

To these we may now add two recent studies. Firstly, Sprung and his colleagues[1] were unable to detect a statistically significant difference in pretreatment lactate concentrations between survivors and non-survivors in a group of patients suffering from septic shock. Secondly, Haupt and her colleagues[2] confirmed the difficulty of attributing prognostic significance to lactic acidosis in septic patients, some patients with high lactate levels showing an ability to increase oxygen consumption in response to fluid loading while others did not; no difference in outcome was observed between the groups.

Thus, we stand by our original conclusion that, on the basis of this study, in shocked, predominantly septic, patients, lactate was a *relatively* unhelpful predictor of outcome and we do not appear to be alone in drawing this conclusion.

Department of Surgery,
Western Infirmary,
Glasgow G11 6NT
I. McA. Ledingham

References

1. Sprung CL, Caralis PV, Marcial EH, Pierce M, Gelbard MA, Long WM, Duncan RC, Tendler MD, Karpf M. The effects of high-dose corticosteroids in patients with septic shock. *New England Journal of Medicine* 1984; **311:** 1137–43.
2. Haupt MT, Gilbert EM, Carlson RW. Fluid loading increases in oxygen consumption in septic patientswith lactic acidosis. *Annual Review of Respiratory Diseases* 1985; **131:** 912–5.

Safe obstetric anaesthesia—just an ideal?

In my travels as a junior locum anaesthetist, and on one occasion as a consultant, I was struck by the variations in the practice of obstetric anaesthesia in the United Kingdom. Variety is the spice of life and it is generally agreed that no two minds think alike. However, when accepted safety procedures are sacrificed to local convention, or to the convenience or whims of the obstetrician, it is a recipe for disaster. Antacid therapy, for example, is generally considered to be a prerequisite for obstetric anaesthesia, whether regional or general. Yet it is often up to the individual anaesthetist to make a positive effort to obtain it. Aortocaval compression, an experienced obstetrician assured me, is all in the minds of the anaesthetist! He only countenanced a right lateral tilt. As for the request for a tilt during a journey, it merely produced puzzled looks. In one maternity unit, cricoid pressure had never been used.

In many centres, including teaching hospitals, it seems impossible to obtain 24-hour skilled help for the anaesthetist. A student midwife with little knowledge of theatre procedure or location of anaesthetic equipment and no experience of cricoid pressure, is often the sacrificial lamb. Failed tracheal intubation under such circumstances could be catastrophic. Given these conditions, discussions on the merits of H_2 'receptor antagonists' seem very academic. An experienced senior anaesthetist might accept variations in standard practice and he, it is to be hoped, can avoid difficulty. The problem arises when the junior anaesthetist is expected to follow the leader. Should the junior get into trouble, it is easy for others to be wise after the event. Perhaps consultant anaesthetists could do more to insist on standard safety practices.

The Report on Confidential Enquiries into Maternal Deaths in England and Wales was first published in 1957. This, and the subsequent triennial reports, have profoundly affected obstetric anaesthetic training and practice in the United Kingdom. However, it appears that the recommendations are not implemented by all maternity units. Should there perhaps be an audit of anaesthetic practices in every maternity unit? Such an audit would reveal any variations that may exist and pave the way for a constructive change. Perhaps the Obstetric Anaesthetists' Association could consider this?

Pain Relief Foundation,
Rice Lane,
Liverpool, L9 1AE
C. Ramamoorthy

Abortions among dental personnel exposed to nitrous oxide

Inhalation-sedation with 35% nitrous oxide in oxygen is popular for the management of anxious undergoing dental treatment. Dental surgeons and their assistants may be exposed to high levels of nitrous oxide during inhalation-sedation therapy.[1] This is most likely if the patient is uncooperative.[2] Exposure to extremely high concentrations is not rare.[3,4] A dose-related abortion rate in dental personnel was reported by Cohen *et al.*,[5] who have extensively reviewed this problem.

Our maxillofacial surgery department has been using this technique for several years. Recently, four female personnel involved with the technique reported six spontaneous abortions out of seven pregnancies during a 17-month period. All abortions occurred during the first trimester. Investigation of nitrous oxide concentrations within the treatment rooms involved revealed some disturbing findings. In the immediate surroundings of the operator and patient, concentrations between 130–400 ppm were measured and, on occasions when the patient talked, peak levels of 700 ppm were registered. Concentrations up to 135 ppm were also registered in the passageway between the two rooms, which are continuously used by personnel. All measured concentrations were higher than those legally permitted for operating theatres in several countries—in Denmark and the U.S.A. this is 25 ppm, in Yugoslavia 5 ppm.

It is impossible to be certain that the high nitrous oxide concentrations were directly responsible for the high incidence of abortions, but there is strong circumstantial evidence for this. We would like to draw the potential dangers of this use of nitrous oxide. Where inhalation-sedation with nitrous oxide is used, precautions should be taken to maintain levels as low as physically possible. Effective expired gas extraction apparatus for use in this situation has been described.[6] Patients should be discouraged from talking during the procedure. Adequate training of personnel is essential. Female personnel who wish to become pregnant should be given the opportunity not to work in rooms where the technique is carried out.

Department of Anaesthesiology, H.C. Schuyt
Academic Medical Centre K. Brakel
of the University of Amsterdam S.G.L.M. Oostendorp
Meibergdreef 9, B.J.M. Schiphorst
1105 AZ Amsterdam,
The Netherlands

References

1. Whitcher CE. Levels of exposure to trace anesthetic gases. In: Cohen EN, ed. *Anesthetic exposure in the workplace.* PSG Publishing Company Inc. USA, 1980.
2. Badger GR, Robertson CW. Nitrous oxide waste gas in the pedodontic operatory. *Journal of the American Dental Association* 1982; **104:** 480–1.
3. Scheidt MJ, Standford HG, Ayer WA. Measurement of waste gas contamination during nitrous oxide sedation in a non-ventilated dental operatory. *Anesthesia Progress* 1977; **24:** 38–42.
4. Jensen SJ, Poulsen S, Bendtsen J, Hansen I. Et udsugningsudstyrs effect på koncentrationen af kvaelstrofforilte i tandlaegens inåndningszone. (Effect of the exhaust device on the concentration of nitrous oxide in the breathing zone of the dentist). *Tandlaegebladet* 1980; **84:** 313–8.
5. Cohen EN, Brown BW, Wu ML, Whitcher CE. Brodsky JB, Gift HC, Greenfield W, Jones TW Driscoll EJ. Occupational disease in dentistry and chronic exposure to trace anesthetic gases. *Journal of the American Dental Association* 1980; **101:** 21–31.
6. Hallonsten AL. II An evaluation of a local exaust system. In: Anna-Lena Hallonsten, ed. *Nitrous oxide–oxygen sedation in dentistry.* Linköping University Medical Dissertations no. 140, Linköping, Sweden, 1982.

Oxygen concentrators

The report by Dr J.A. Carter and colleagues (*Anaesthesia* 1985; **40:** 560–5) was most interesting. From our experience in Chester, with a hospital size oxygen concentrator system, I would like to make one or two comments. The artificial zeolites that form the molecular sieve do not distinguish between the molecules of oxygen and argon, while all other gases are removed from air. Both oxygen and argon are concentrated. In our experience, the resultant mixture of gases does not exceed 95.7% oxygen, 4.3% argon, and less than 0.1% nitrogen (all v/v), when the concentrator is operating optimally. The highest argon levels found did not exceed 5.5%. When the oxygen concentration falls, there is a corresponding rise in nitrogen concentration. Unless the zeolite used in the 'Permox' has unusual properties, the suggestion that the maximum oxygen concentration obtainable is 99% is misleading. Oxygen analysers are susceptible to drift, a major component of which are local variations in barometric pressure. An uncompensated Taylor Servomex Type 570A paramagnetic oxygen analyser was used to operate the 'oxygen % out of range' (that is, the oxygen concentration has decreased to 92% and may still be declining) alarm on the outlet side of the oxygen storage vessel at the Countess of Chester Hospital and this produced a number of false positives. The indicated concentration fluctuated with local atmospheric pressure variations. It was noticeable that the opposite condition of over-reading bothered us far less! The oxygen concentration did not fall below 92.9% and was usually within a few tenths of one per cent of 95%.

The artificial zeolites absorb water, but if the air entering the absorption chamber is not dry, there is steady deterioration and loss of performance in adsorbing nitrogen. The water also has a deleterious effect on the molecular sieve material, causing a steady attrition. It is preferable to use dry air.

The actual 'Permox' oxygen concentrator unit is without mechanical or electrical components, but it does need the compressor unit which is electromechanical. Failure of the compressor at present appears to be the major point of weakness in oxygen concentrator systems, particularly if they are run at maximum capacity continuously. Cooling for the compressor is vitally important and, if inefficient or ineffective, leads to breakdown of the system. Intermittent bursts of use are less likely to cause compressor failure.

Department of Anaesthetics, D. Lush
Countess of Chester Hospital,
Liverpool Road,
Chester CH2 1BQ

Atracurium and vecuronium in emergency eye surgery

When an unprepared patient presents for emergency surgery the risk of aspiration of gastric contents can normally be reduced by employing an accelerated induction technique, which includes the use of suxamethonium to facilitate rapid intubation of the trachea. However, in the patient with a perforating eye injury, suxamethonium is contraindicated because it causes a rise in intra-ocular pressure (IOP),[1] with the risk of extrusion of intra-ocular contents. Non-depolarising muscle relaxants offer an alternative, but their slower onset of action lengthens the period of risk before the trachea can be intubated. This period can be reduced if the relaxant is given prior to induction of anaesthesia although the relaxant–induction interval must not be so long that the patient becomes aware of the onset of paralysis before losing consciousness. An interval of 30 seconds has been found to be satisfactory in a previous study using fazadinium (R.J.E., in press).

Atracurium and vecuronium are non-depolarising muscle relaxants promoted as having a rapid onset of action and suitable for facilitating intubation when suxamethonium is contraindicated.[2] It was felt therefore, that their potential should be examined to see if rapid intubation could be achieved without an accompanying rise in IOP.

Thirty-seven adult patients (ASA class 1 and 2) undergoing routine eye surgery were randomly allocated to receive either atracurium or vecuronium. Ninety minutes after they had received a standard premedication consisting of diazepam 10–15 mg the resting intraocular pressures were measured using a Perkins applanation tonometer. The allotted muscle relaxant was administered through an intravenous infusion (atracurium 0.6 mg/kg or vecuronium 0.1 mg/kg) after pre-oxygenation. These are recommended as suitable, and approximately equipotent, doses.[2] Thirty seconds later, anaesthesia was induced with thiopentone 5 mg/kg and one minute afterwards the trachea was intubated. Intubating conditions were compared using a modification of the scale introduced by Lund and Stovner.[3]

The patient's lungs were then inflated using a Bain

Table 1. Comparison of intubating conditions ($p < 0.05$, Chi squared test)

	Number of patients		
Intubating conditions	Atracurium group	Vecuronium group	
No reaction	11	4	satisfactory
Movement of cords, no bucking	1	2	
Slight bucking	3	5	unsatisfactory
Severe bucking	3	8	
Intubation impossible	0	0	

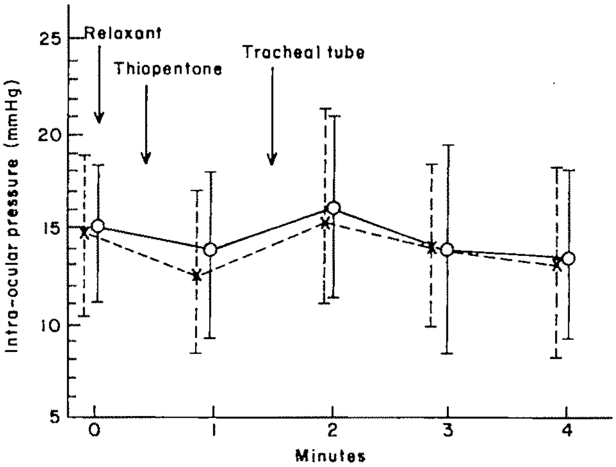
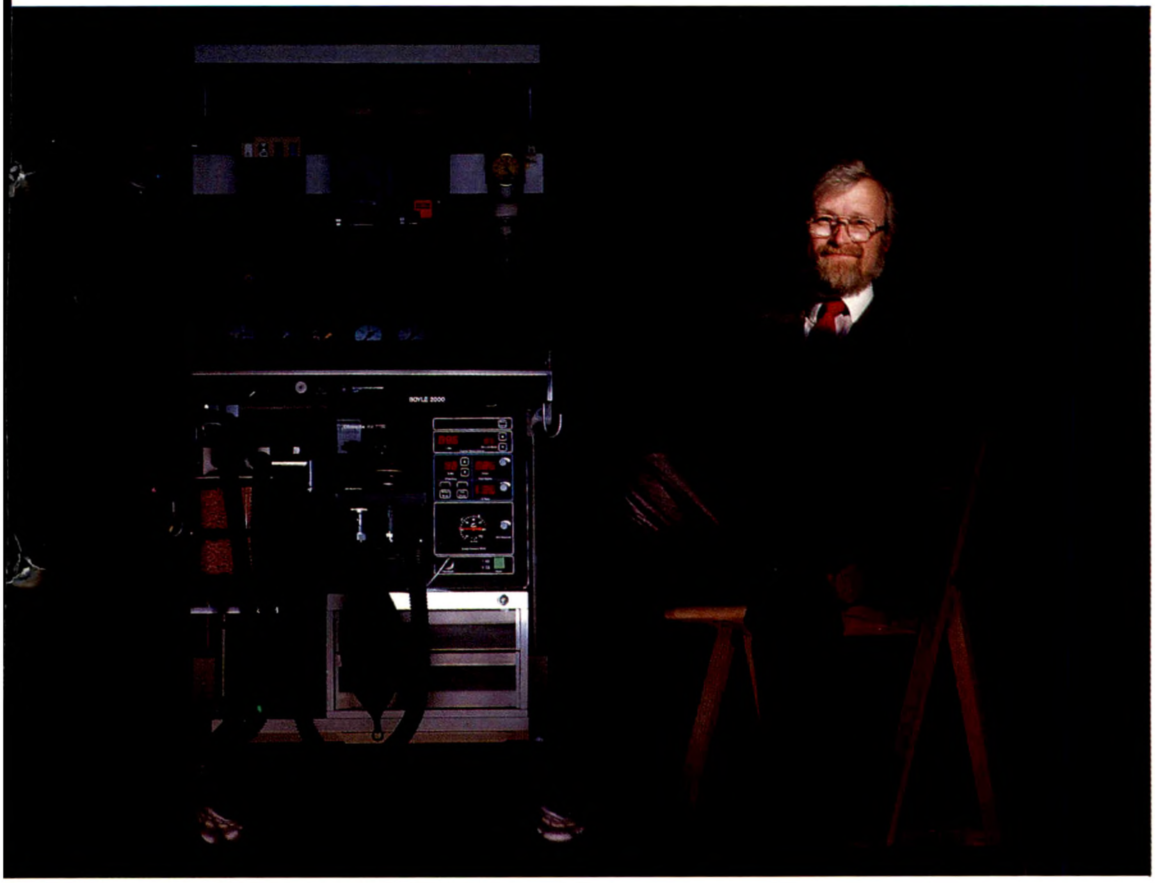


Fig. 1. Mean IOP (SD). (o), Vecuronium; (x), atracurium.



Ventilation takes a step forward.

Working closely with the anaesthesia profession worldwide for more than 60 years, Ohmeda has developed some of the world's finest medical equipment.

Our joint efforts have produced a formula that has worked effectively, and the results are evident in our latest development: the OAV 7700 anaesthesia ventilator.

One of the most advanced anaesthesia ventilators available to date, the OAV 7700 offers the accuracy of electronic control combined with the reliability of pneumatically operated lung ventilation.

A highly flexible unit, the OAV 7700 can be used in either open or closed circuit applications. This unit also offers fully integrated alarms and a clear and immediate display of all patient breathing parameters.

Used in conjunction with the Boyle 2000 or International 2 anaesthesia machines, the OAV 7700 becomes part of a highly reliable, easy to use, cost effective anaesthesia system. One designed with your help . . . to meet your needs.

Specify Ohmeda — We won't let you down.

SPECIALIST CARE FOR SPECIALIST PEOPLE.

Ohmeda

Ohmeda
Elizabeth Way Harlow Essex CM19 5AB England
0279 29692 Telex 81497

BOC Health Care

ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND

TRAVENOL TRAVELLING FELLOWSHIP

Applications for the 1986 award (£2,500) are invited now, and should be sent to the Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA, by 1st March, 1986. Details are to be found in the News and Notices Section of this issue.

HEINEMANN MEDICAL

PRACTICAL
ANAESTHESIA
FOR SURGICAL
EMERGENCIES

Edited by Peter W. Jackson

'This little book should be available in every resident anaesthetist's bedroom. It will do good.' Anaesthesia

This highly practical pocketbook contains a set of guidelines for each clinical situation, with a clear statement of the rationale of each step.

122pp, 186 x 123mm, limp, illus **£8.95**

NEW
Anaesthesia in the Elderly

Harold T. Davenport
Foreword by Sir Gordon Robson

'Half of all patients over 65 will have an operation before they die.'

This book covers those practical aspects of anaesthesia management which are likely to influence the standard of care of the elderly. Particular attention is devoted to the care of chronic pain and the palliation of terminal disease.

196pp, 216 x 138mm, limp, illus **£10.95**

WILLIAM HEINEMANN MEDICAL BOOKS
23 Bedford Square, London WC1B 3HH **(01) 637 3311**

system with a mixture of nitrous oxide 4 litres/minute and oxygen 2 litres/minute and the IOP was measured at one-minute intervals throughout the study period of four minutes, after which anaesthesia proceeded according to the anaesthetist's normal practice. The age, sex, weight and resting IOP of the patients in both groups were very similar. Ninety seconds after administration of the relaxants, it was possible to intubate all the patients. Reactions to intubation were encountered in some patients in both groups, but conditions were significantly ($p < 0.05$) better in the atracurium group (Table 1).

In Fig. 1, the mean IOP (SD) is plotted at one-minute intervals throughout the induction sequence. In both groups, it fell following induction and was at its highest immediately after intubation, at which time it exceeded resting values. There was no significant difference between the two groups (Student's *t*-test). The results show that rapid intubation was possible following both relaxants, but that when performed within ninety seconds of administration, the conditions for intubation were not always satisfactory and there was sometimes an accompanying rise in IOP. Therefore neither drug, when given in the manner described, could be recommended for the unprepared patient with a perforating eye injury.

Department of Anaesthetics,
Gloucestershire Royal Hospital,
Great Western Road,
Gloucester

S. MALLAIAH
R.J. ELTRINGHAM
D.M. MAGAURAN

References

1. PANDEY K, BADOLA RP, KUMAR S. Time course of intraocular hypertension produced by suxamethonium. *British Journal of Anaesthesia* 1972; **44**: 191–5.
2. SCHILLER DJ, FELDMAN SA. Comparison of intubating conditions with atracurium, vecuronium and pancuronium. *Anaesthesia* 1984; **39**: 1188–91.
3. LUND I, STOVNER, J. Experimental and clinical experiences with a new muscle relaxant RO4-3186 diallyl-nor-toxiferine. *Acta Anaesthesiologica Scandinavica* 1962; **6**: 85–97.

Susceptibility to malignant hyperpyrexia

We are surprised Dr Moxon (*Anaesthesia* 1985; **40**: 693–5) has taken such a narrow view of the importance of the diagnosis of malignant hyperpyrexia susceptibility (MHS) in her article. Our unit has been quoted several times so please permit us to comment.

Case 1. With no septic focus, a temperature of 39°C with a mixed acidosis and hyperkalaemia, all controlled by dantrolene, must indicate a provisional diagnosis of MH in this 25-year-old male. The fact that he opted out of further investigation is of no great concern, since he can be given a Medic Alert medallion stating the likely diagnosis.

But what of his family? It has been well documented that creatine phosphokinase estimations do not help in this circumstance[1,2] so why does Dr Moxon base her phenotyping on an outmoded test? Is she suggesting that the patient's MH was not inherited if the CPK values in his family '... were apparently normal ...'? How would she feel if another case—possibly fatal—occurred in an unwarned branch of the proband's family?

Case 2. Pre-operative pyrexia due to rectal abscess is likely to increase with surgery which inevitably increases the spread of pyrotoxins with physical manipulation. Even with this pyrexia, serum potassium was low normal at 3.5 mmol/litre and myoglobinuria did not develop. A respiratory acidosis after gallamine 15 mg with 3% halothane in a Magill attachment is hardly surprising. A negative muscle biopsy result is therefore fully comprehensible and must be something of a relief to both the patient and other members of his family.

Case 3. If this patient developed an aborted form of MH, her presentation of '... felt like death ...' after halothane must be unique. Dr Moxon does not give any blood gas, serum potassium or urine analysis findings, so it would be impossible for any reader of her article to have any opinion. This is the type of patient who should be considered for muscle biopsy to clear up a diagnostic quandary.

It may be relevant to point out that a hospital administration will pay for a proband to be investigated in a distant unit if the referring hospital does not have the necessary expertise. Dr Moxon's comment about the travel being 'almost impossible financially' could only refer to secondary family members and not to the patient she quotes (Case 3). Furthermore, she incorrectly quotes our policy. We always prefer to investigate a proband so as to confirm the diagnosis, but if the proband dies, or is too young or too ill or refuses to attend, we will always accept other family members; preference is given to parents, children and siblings who carry a 50% probability compared with the proband.

Anaesthesia for a susceptible patient should be straightforward provided trigger agents are not used. However, if patients are not investigated, all family members must be considered to be at risk, and all family members must receive a 'trigger-free' anaesthetic. Some surgeons and also some anaesthetists are reticent to accept MHS patients as reasonable operative risks. If a patient is shown on testing to be normal, we believe strongly that this patient should be treated as a normal individual. In our experience, no 'normal' patient who has been given trigger agents has subsequently developed MH. Comments about patients developing suxamethonium spasm have been misquoted and apparently misinterpreted.[3]

Although we regret the soreness resulting from the muscle biopsy, we feel the advantages of a precise diagnosis far outweigh this temporary inconvenience.

University Department of Anaesthesia, F.R. Ellis
St James's University Hospital, P. Jane Halsall
Leeds, LS97TF

Reference

1. Ellis FR, Clarke IMC, Modgill M, Currie S, Harriman DFG. An evaluation of creatinine phosphokinase in screening patients for malignant hyperpyrexia. *British Medical Journal* 1975; **3:** 511–3.
2. Gronert GA. Malignant hyperthermia. *Anesthesiology* 1980; **53:** 395–423.
3. Ellis FR, Halsall PJ. Suxamethonium spasm. A differential diagnositic conundrum. *British Journal of Anaesthesia* 1984; **56:** 381–4.

A reply

Thank you for the opportunity to reply to the letter from Dr Ellis and Dr Halsall. The purpose of the article was not to take a narrow view of the diagnosis of malignant hyperpyrexia, but rather to discuss some of the problems which continue to arise in a District General Hospital, despite the excellence of the service given by Dr Ellis and his colleagues in Leeds.

Case 1 was a man who had recently come to live to live in our area and all his relatives are still 300 miles away. The medical staff in that area were given full information about his suspected diagnosis, and told of his reluctance to go to Leeds. The CPK values of the rest of the family were then sent to us and, although no further investigations were planned, the relatives were all given Medic Alert bracelets. This worry about relatives and what information they should be given is one of the concerns of this paper.

The clinical episode in case 2 was very difficult. It was a dramatic incident and witnessed by a senior colleague who had been present at a proven MH crisis before. She too considered that it was a probable MH crisis at the time, and the negative biopsy both surprised and pleased us but left a diagnostic conundrum.

With reference to case 3, it is unfortunate that blood and urine investigations were not done at the time of the reported incident, because junior medical staff saw the patient and did not realise the possible significance of the symptoms. Her own comment, 'felt like death', seemed very apt, as it was exactly the phrase used by another patient (a proven MH case) to describe the way he felt after a halothane anaesthetic. Whilst the hospital administration may be willing to pay expenses for the patient (and this is not always the case), they would not pay for an accompanying relative or friend. A young mother with a self-employed husband could still have considerable financial problems.

The advantages of a precise diagnosis are not disputed. The presentation of the cases and discussion were to highlight some of the associated problems encountered by patients, relatives and their anaesthetists.

Department of Anaesthetics, M.A. Moxon
Royal Berkshire Hospital,
London Road,
Reading,
Berkshire RG1 5AN

Tracheal tube obstruction by prominent aortic knuckle

Having recently read with interest Dr Sapsford and Dr Snowdon's case report (*Anaesthesia* 1985; **40:** 5524) which suggested a prominent aortic knuckle as an extraluminal cause of tracheal tube obstruction, we would like to describe a similar case we recently encountered.

An 86-year-old man with ischaemic heart disease and moderate chronic obstructive airways disease had undergone a 3-hour laparotomy for resection of large bowel and fashioning of a colostomy (following a diagnosis of strangulated femoral hernia). Anaesthesia was uneventful and, in particular, no ventilatory problems were encountered. Intermittent positive pressure ventilation (IPPV) was through a 9.0 mm cuffed Portex disposable tracheal tube. Neostigmine and atropine were administered at the end of the procedure, to reverse muscle paralysis and the patient was turned to the right lateral position prior to extubation. Two events took place: ventilation of the lungs was difficult, manual ventilation using a a Bain system with 100% oxygen resulted in little air entry to the lungs, and supraventricular tachycardia (SVT) had developed.

It was decided to re-institute muscle relaxation (using vecuronium) with a view to continued ventilatory care postoperatively. When the patient was turned to the supine position, the difficulty with ventilation disappeared completely. Verapamil was administered to treat the SVT. The patient was now stable and spontaneous ventilation was adequate, so a reappraisal of the situation was made. The pre-operative chest X ray showed an almost identical picture to that in the aforementioned article; the trachea was deviated to the right and its diameter reduced at the level of a prominent aortic knuckle. We noted that if the tracheal tube was advanced about 2 cm, ventilation became difficult; also, if the patient's head was turned to the right, a similar difficulty ensued.

Flexible bronchoscopy demonstrated a marked indentation in the tracheal wall to the left, and prominent transmitted pulsation was noted. The left main bronchus could not be seen until the flexible bronchoscope tip was manoeuvred past the obstruction. IPPV was continued rather than reversal of muscle relaxation (in view of the previous episode of SVT). Difficulty with tracheal suction was also a problem during the postoperative ventilatory period: manipulation of the tracheal tube, and the patient's head, were necessary in order to manoeuvre the suction catheter past the obstruction.

Dr Sapsford and Dr Snowdon did not bronchoscope their patient for justifiable reasons. Our case, however, backs up their theory that the aortic knuckle can indeed cause a significant degree of extrinsic tracheal compression. Their suggestion that 'when in doubt take it out' we feel was not wholly applicable in this case, where the problem did not manifest itself until 3 hours after intubation.

Department of Anaesthesia,
Ninewells Hospital,
Dundee DD1 9SY

J. MARTIN
B. HUTCHISON

Local analgesic convulsions and epidural analgesia for Caesarean section

The recent article by Thompson *et al.* (*Anaesthesia* 1985; **40:** 427–32) was most interesting, since it attempts to put on a scientific basis a clinical problem which faces obstetric anaesthetists with increasing frequency; that is, the provision of regional analgesia for Caesarean section without the risk of toxic effects in the mother or her fetus from the local anaesthetic. The authors used four variations on an incremental theme (three of these were in elective and the fourth was in emergency Caesarean section patients). Probably, all these techniques are in common clinical use. Despite this, in 35% of patients (11 out of 31) in two of the elective groups, the dose required exceeded the manufacturer's recommended safe limit and blood bupivacaine levels were above the accepted threshold for toxic effects in 77% (34 out of 44) of estimations in the emergency group.

It is clear from these figures, and this will hardly surprise most practising obstetric anaesthetists, that the dimensions and complexity of the epidural space are such that in obstetric patients it is not always easy to obtain satisfactory analgesia for Caesarean section by injection through an epidural catheter. Successful analgesia can often be achieved in recalcitrant cases by exceeding and the manufacturer's recommended safe dosage of bupivacaine and, while such a technique has been advocated,[1] the risks of doing so have been highlighted by the recent description of convulsions resulting from local analgesic overdose in two patients.[2] These two cases were reported from one hospital, so it would be very surprising if others had not occurred.

If toxic reactions, or even fatalities, are to be avoided in the future, safer alternatives must be employed than the simple injection of incremental doses of a local anaesthetic through the epidural catheter at one point in the epidural space. Apart from recourse to general anaesthesia, an alternative which not only introduces additional hazards but is usually a great disappointment to the patient, there are three alternative regional anaesthetic techniques which may be used.

The epidural catheter may be withdrawn slightly or another catheter inserted at a more cephalic lumbar interspace. This somewhat empirical approach is sometimes successful for extending an epidural block, but may require a potentially dangerous volume of local analgesic if the toxic dose has already nearly been reached. This is not a particularly safe alternative, since it may not always be effective.

A thoracic epidural catheter may be inserted. Most epidural blocks for Caesarean section that are inadequate, are so because the block is not high enough. The insertion of a catheter in the middle of the unblocked area, for example at the T_{8-9} or T_{9-10} interspaces, reliably completes the analgesia with as small a volume of local anaesthetic solution as 5–6 ml.

A subarachnoid block may be substituted. The volume of local analgesic required is so small as to have virtually no effect on the plasma level. The spinal method is preferred when the extent of the block provided by the lumbar epidural is so limited or patchy that it seems unlikely that the required analgesia can be achieved with a small dose of local analgesic in the thoracic epidural space. Hypotension is less marked than when spinal analgesia is used alone, because sympathetic blockade has already been induced to a considerable extent by the epidural blocks.

It should be possible, with these alternatives in mind, to provide effective regional analgesia for almost any Caesarean section without transgressing the recommended safe dose of local analgesic, and obstetric anaesthetists should be able to perform these alternative techniques.

Maternity Department,
John Radcliffe Hospital,
Headington,
Oxford,
OX3 9DU

L.E.S. CARRIE

References

1. CRAWFORD JS. 0.75% bupivacaine. *British Journal of Anaesthesia* 1985; **57:** 240.
2. TAHORBURN J, MOIR DD. Bupivacaine toxicity in association with extradural analgesia for Caesarean section. *British Journal of Anaesthesia* 1984; **56:** 551–3.

A reply

In view of these comments on the methods used in our study we emphasise the success of one technique in avoiding toxic bupivacaine levels. In no patient, who received incremental top ups at 20-minute intervals, was the manufacturer's recommended upper limit of dosage exceeded, nor were toxic plasma levels found.

We would agree with the author that there is room for improvement in epidural techniques and welcome his alternative suggestions, however, we have found that the majority of recalcitrant patients accept with relief the suggestion of general anaesthesia.

Department of Anaesthetics,
The Queen's University of Belfast,
Northern Ireland

C.M. Wilson
J. Moore

An alternative to Allen's test

Allen's test, to demonstrate the patency of the ulnar collateral blood supply of the hand, is well established as a precautionary measure prior to the insertion of a radial arterial line. The patient should be awake and cooperative enough to make and to release a clenched fist for this test to be adequate. However, most acutely ill patients admitted to the intensive care unit or operating room are not able to perform this simple manoeuvre. These patients are usually in most need of direct arterial monitoring, so radial cannulae may be inserted without a check of the patency of the ulnar collateral circulation.

It is possible quickly to check the patency of the ulnar collateral circulation in the unconscious patient with a pulse meter, preferably one which displays a trace on an oscilloscope. The pulse detector is placed on the thumb of the hand which is chosen for radial arterial cannulation, and the gain is adjusted on the pulse monitor, so that a satisfactory trace is displayed on the oscilloscope. Both radial and ulnar arteries are compressed at the wrist. The trace will go flat. When the pressure on the ulnar artery is released, the trace reappears if the ulnar artery is patent. Failure to demonstrate an ulnar trace suggests that the ulnar collateral circulation is inadequate, and that another site be chosen for arterial cannulation.

Royal Preston Hospital,
P.O. Box 66,
Sharoe Green Lane,
Preston PR2 4HT

P.W. Duncan

Petechial rashes and automatic blood pressure measurement

The recent case described by de Silva and Mostafa (*Anaesthesia* 1985; **40:** 817) in which a petechial rash in the elbow followed the use of a Dinamap blood pressure machine raises an important point of management. We have had one case in which the entire forearm developed a petechial rash in a fit 40-year-old woman undergoing elective urological surgery without evidence of a coagulation or platelet disorder. We believe that in this case, the problem occurred because of the repeated cycling of the machine to search for a high systolic pressure without full cuff deflation. A quite separate problem has occurred in ITU, where there has been a spate of presumably traumatic purpura on the skin directly underneath the inflating cuff. All these cases have occurred with machines other than the one used by de Silva. The incidence in ITU is less than 5%, but appears to be more common in the obese arm and when high inflation pressures have to be used. There is no evidence that patients with bleeding disorders, which constitute a significant input into this unit, are more prone to this problem than any other. To minimise its development, we employ a regular change of cuff from arm to arm and a Tubigrip sleeve placed under the inflation cuff. It is difficult at this stage to know the success of such manoeuvres. We believe all these problems are due to the sustained inflation of the tourniquet for too long a period when a high systolic pressure is sought. The problem needs a fuller evaluation, but manufacturers should take note of an additional safeguard we believe should be introduced into all these machines.

Department of Anaesthesia,
Freeman Hospital,
Newcastle upon Tyne, NE7 7DN

B.J. Nicholls
D.W. Ryan

Epidural meptazinol

Following a recent report claiming success with the use of extradural meptazinol,[1] we wish to present our own findings.

Our study was designed to assess the efficacy and safety of extradurally administered meptazinol following Caesarean section. The trial was conducted in an open fashion, the mothers being randomly assigned to receive either epidural meptazinol 30 mg or intramuscular papaveretum as a control. Standard exclusion criteria were applied and all mothers gave informed consent. Caesarean section was carried out under epidural anaesthesia using an incremental technique.[2] Meptazinol was administered at the time of skin closure. Controls received papaveretum as requested.

Respiratory function was continuously monitored over the following 12 hours by means of a specially developed impedance pneumograph,[3] which, in unpublished work, has been shown to be accurate (less than 10% error) for short and long term work. Breath-by-breath impedance data is analysed in real time by a microcomputer, to give mean tidal and minute volumes every 30 seconds and 5 minutes. The respiratory rate is also continuously analysed, and periods of apnoea and bradypnoea are registered and counted. Every 5 minutes the averaged tidal volume, respiratory rate, apnoea and bradypnoea counts are saved to floppy disc for later analysis.

The first four patients were controls. The mean minute volumes varied considerably, but no episodes of apnoea or bradypnoea were detected, no side effects were encountered and all the patients reported good or very good analgesia by verbal rating score. Patients five to seven received epidural meptazinol. Patient five reported severe itching by 9 hours, but good analgesia. Two brief periods of bradypnoea were also detected at 7 hours after injection. Patient six suffered severe nausea and vomiting at one hour which responded poorly to anti-emetics. Her pain relief was rated as fair. Patient seven experienced poor pain relief and at 4 hours developed severe nausea, dizziness and sweating. Her blood pressure rose from 130/80 to 155/105 mmHg. She developed peripheral oedema and had difficulty breathing. She was given sympomatic treatment and was withdrawn from the trial. The side effects lasted for about half an hour. In view of these poor results the trial was abandoned and one further patient was given meptazinol. This eighth patient reported only fair analgesia, and at about 4 hours suffered severe nausea and vomiting. She had two periods of bradypnoea at 3 hours. Patients five, six and eight each required a supplemental parenteral dose of meptazinol at between 3 and 4 hours from the end of surgery. The duration of analgesia in the control group ranged from 2.5 to 13 hours, and in the meptazinol group from 3 to 4 hours.

Two obvious conclusions can be drawn although our group is not a statistically valid population. Firstly, we failed to produce adequate analgesia with epidural meptazinol and secondly, the incidence of serious side effects was far too high. In view of these findings, we feel that the use of meptazinol by the epidural route should be actively discouraged, and the drug not licensed for this use.

The Birmingham Maternity Hospital, R.I. Francis
Birmingham, B15 2TG A.S. Lockhart

References

1. Rao U, Campbell IT, Catley DM, Sutherst JR. Postoperative analgesia with extradural meptazinol: an open dose-finding study. *British Journal of Anaesthesia* **57**: 814–5P.
2. Crawford JS. *Principles and practice of Obstetric Anaesthesia*, 4th Ed. Oxford: Blackwell Scientific Publications, 1978; 262–3.
3. Francis RI, Hollins G. B.M.H. Respiratory monitor. *Anaesthesia* 1985; **40**: 97.

Non vagolytic anaesthetic sequence—sinus arrest

We note with interest the letters of Dr Macrae and Dr May on the subject of bradydysrhythmias during anaesthesia, when vecuronium is used. (*Anaesthesia* 1985; **40**: 710). Sinus arrest has also occurred in two previously reported incidents.[1,2] We consider that these reports are important, both as a warning to other users of a common anaesthetic technique and so that in the longterm any common factors in these cases can be firmly established. We would like to report a further two cases of transient sinus arrest which have occurred when vecuronium was in use.

Case 1. A 70-year-old asthmatic lady on 5 mg prednisolone a day and Intal was anaesthetised for elective cholecystectomy. Pre-operatively she received aminophylline suppositories, hydrocortisone 100 mg, promethazine 25mg and pethidine 50 mg as premedication. Tracheal intubation was uneventful and anaesthesia was maintained with nitrous oxide, oxygen and halothane. Five mg vecuronium was given after transfer into theatre and recovery from suxamethonium. Fifteen minutes later, while the hiatus was being examined for hernia by the surgeon, bradycardia was followed by sinus arrest. Nitrous oxide and halothane were discontinued and oxygen flow increased to 8 litres/minute; 0.6 atropine was given intravenously and cardiac massage was instituted with manual ventilation of the lung. ECG showed regular complexes again after about 10 massage beats and systolic blood pressure was 130 mmHg. The remainder of the operation and recovery period were uneventful.

Case 2. An unpremedicated, previously fit, 19-year-old girl was given a general anaesthetic for emergency appendicectomy. Following pre-oxygenation for 3 minutes, anaesthesia was induced with thiopentone 275 mg and after relaxation with 100 mg suxamethonium, a cuffed orotracheal tube was inserted under cricoid pressure. Nitrous oxide, oxygen and halothane were used to maintain anaesthesia. The patient was transferred into theatre and connected to a ventilator and ECG monitor. Signs of recovery from suxamethonium were evident and vecuronium 6 mg and papaveretum 10 mg were given intravenously as boluses. Surgery had not yet commenced. A few seconds after this, attention was drawn to a flat ECG tracing by the alarm, several seconds of asystole were followed by the spontaneous appearance of isolated normal complexes, then by sinus bradycardia of about 20 beats/minute of sinus rhythm, which responded promptly to atropine. The patient's colour remained satisfactory throughout and the operation was commenced, and completed, uneventfully and included a further increment of 2 mg vecuronium.

Minor bradycardias, rate under 50/minute, are probably seen frequently by regular users of vecuronium. An early study noted 10 cases out of 200, about 20 minutes after administration of the drug.[3] Severe bradydysrhythmias have been observed in nine cases during eight consecutive operating sessions for eye surgery.[4] A similar pattern of response is emerging with atracurium, 19 cases out of 626 cases in one series,[5] and in nine out of 68 cases in another.[6] In addition, there have been four cases reported of severe bradycardia[7] and two cases of asytole for 15 seconds during gynaecological surgery.[8]

We admit that in none of these reports is there any evidence that bradydysrhythmias were directly attributable to the neuromuscular relaxants in a pharmacological sense. The contributory factors were the use of halothane and opiates and the effects of vagal stimulation in the absence of anticholinergic drugs. Our first patient was receiving halothane and the vagus was being stimulated at the time. In the second case, halothane and papaveretum had been administered and as postulated in a recent report,[9] a Valsalva effect during the recovery of muscle tone and during intermittent positive pressure ventilation of the lungs is a possibility.

The blamelessness of the new neuromuscular blockers in causation of these bradydysrhythmias is perhaps in a certain sense irrelevant; the important fact remains that bradydysrhythmias are occurring during surgery with common anaesthetic techniques (including enflurane and isoflurane anaesthetics,[3,4,9–11] when the non vagolytic atracurium and vecuronium are used as neuromuscular blockers. The complete cardiac 'cleanliness' of the new drugs is thus a disadvantage. There is debate about the significance of even fairly extreme bradycardia when the patient appears otherwise well, but most anaesthetists will probably agree that complete asystole is thoroughly undesirable. Since there is no way at present of distinguishing those patients who are susceptible to bradycardia, nor those few who progress to sinus arrest, then perhaps as suggested by Dr May and others, an anticholinergic agent should be routinely employed when using vecuronium or atracurium.

Finally, is it possible that while the neuromuscular blockers have no direct cardiac action, they act to make some invididuals more susceptible to vagal or parasympathomimetic activity?

Anaesthetic Department, M. Higgins
Monklands District General Hospital, J.M. Thorp
Airdrie ML6 OJS

References

1. Kirkwood I, Duckworth RA. An unusual case of sinus arrest. *British Journal of Anaesthesia* 1983; **55:** 1273.
2. Milligan KR, Beers HT. Vecuronium-associated cardiac arrest. *Anaesthesia* 1985; **40:** 385.
3. Mirakhur RK, Ferres CJ, Clarke RSJ, Bali IM, Dundee JW. Clinical evaluation of Org NC45. *British Journal of Anaesthesia* 1983; **55:** 119–24.
4. Pryne SJ, Edwards JC. Vecuronium and the oculocardiac reflex. *Anaesthesia* 1985; **40:** 88–9.
5. Rowlands DE. Correspondence on 'bradycardia after the use of atracurium'. *British Medical Journal* 1983; **287:** 760.
6. Didier H. Atracurium without bradycardia. *British Medical Journal* 1983; **287:** 984–5.
7. Carter ML. Bradycardia after the use of atracurium. *British Medical Journal* 1983; **287:** 247–8.
8. Lawler PGP, McHutchon A. Correspondence on bradycardia after the use of atracurium. *British Medical Journal* 1983; **287:** 759–60.
9. Hardy PAJ. Atracurium and bradycardia. *Anesthesia* 1985; **40:** 504–5.
10. Williams HD, Studd C. Vecuronium bromide and complete atrioventricular block. *Anaesthesia* 1985. **40:** 205.
11. May JR. Vecuronium and bradycardia. *Anaesthesia* 1985; **40:** 710.

More on combined subarachnoid and epidural techniques

Recent publication on this technique[1] prompts me to report a very interesting phenomenon one may encounter when this technique is undertaken. The technique suggested by Coates[2] and later modified by Nickalls and Dennison[3] for obstetrics, lower abdominal, perineal and lower extremity operations is used. The epidural space is located by the loss of resistance to air and a spinal block is performed with a 26 SWG needle. Later, when the epidural catheter is threaded, a minute quantity of clear, or slightly red-tinged fluid sometimes comes back through the catheter. An aspiration test from the catheter has always been negative. Whenever this leakage happens, the expected level of anaesthesia is not achieved. On the majority of occasions, after careful observation, the block was extended with an epidural injection. No untoward incident has been observed after epidural dose.

The source of this minute quantity of fluid is either cerebrospinal fluid or local anaesthetic agent. There has been no incident or very high block or of spinal headache and, since an epidural injection extended the block, one suspects that the minute quantity of fluid is anaesthetic agent. Local anaesthetic may be deposited in the epidural space if the spinal needle has travelled too far, out through the dura, or as a result of movement of the needle in and out of the dura during the period of injection. There is a theoretical possibility that the catheter might enter the intrathecal space through the hole made in the dura by the spinal needle, but this has not been reported. The above evidence is in the favour of fluid being local anaesthetic agent.

It is concluded that drip back of fluid may be encountered in the combined spinal and epidural catheter technique occasionally. It should not cause alarm and aspiration should be performed before an epidural drug is given to extend the block, if this is required.

Department of Anaesthesia,
South Cleveland Hospital,
Marton Road,
Middlesbrough, Cleveland

C.M. Kumar

References

1. Crampton Smith A. More on combined subarachnoid and epidural techaniques. *Anaesthesia* 1985; **40:** 823.
2. Coates MB. Combined subarachnoid and spinal techniques. *Anaesthesia* 1982; **37:** 89–90.
3. Nickalls RWD, Dennison B. A modification of the combined spinal and epidural technique. *Anaesthesia* 1984; **39:** 935–6.

Accidental disconnexion following inactivation of Servoventilator alarm

We wish to draw attention to the dangerous practice of adjusting the lower limit of the expired minute volume alarm to zero on the 900 series Servoventilators. This inactivates the loud alarm which provides warning of disconnexion and, if staff are tempted to cancel it in this way, it is silenced permanently. We are aware of two patients who, because of this practice, were rendered sufficiently hypoxic to develop bradycardia following accidental disconnexion. Each incident followed prolonged chest physiotherapy by experienced intensive care staff, during which the lower alarm limit control was set to zero. The patient was insecurely connected to the ventilator after physiotherapy and disconnexion followed. Hypoxia and bradycardia were corrected after reconnexion and no permanent damage ensued.

Deliberate inactivation of alarm systems is a well recognised problem;[1,2] nevertheless, discussion with colleagues suggests that specific measures to prevent this are rarely employed. The Siemens ventilator manual clearly describes the function of the lower alarm limit but the hazard of a zero setting is not emphasised. There is, however, a warning light on the console to indicate that the alarm is effectively inactivated, but a small flashing light can easily go unnoticed in a busy ward. Siemens Ltd have stated that they encounter this difficulty only rarely and they are confident that most users are aware of the problem. The two incidents described here, however, suggest this is not always the case. Nurses are trained to use the 2-minute delay button during physiotherapy, but it is unrealistic to expect this rule to be followed invariably. Disconnexion does occur and the presence of a silenced alarm is especially hazardous since it gives a false sense of security. Ideally, it should be impossible permanently to inactivate an alarm when the ventilator is in use.

The solution which we have adopted for all our Servoventilators is to incorporate a 'stop' which prevents the lower alarm limit being set to zero. We understand that Siemens have similarly modified a few ventilators on request. We believe that, in the interests of patient safety, this modification should be universally adopted.

Department of Anaesthesia,
St Bartholomew's Hospital,
West Smithfield,
London EC1A 7BE

M.R.J. Sury
C.J. Hinds
M. Boustred

References

1. Altman P, Pumphrey D, Bailey WC. Modification to prevent deactivation of Bennet Spirometer Alarm System during mechanical ventilation. *Respiratory Care* 1973; **18:** 294–5.
2. Fodor I, Bloomfield D, Fisher A, Kerr JH. A control-free ventilator alarm. *Anaesthesia* 1977; **32:** 1026–9.

Tonsillar enlargement and palatal surgery

A recent report of airway obstruction after cleft palate surgery in a child with Pierre Robin syndrome[1] prompts are to report a similar, but potentially more common, problem that I encountered recently.

The patient was a 5-year-old child who, 4 years after a repair for cleft palate, was noted to have a posterior palatal fistula and was scheduled for closure of the fistula and lengthening of the soft palate. He was known to have beta thalassaemia trait and was rather small for his age (16 kg), but further examination was normal. He was seen pre-operatively and noted to be free from any upper respiratory tract infection.

An uneventful inhalational induction with oxygen, nitrous oxide and enflurane, tracheal intubation with a size 5 mm Oxford tracheal tube, facilitated by suxamethonium 12.5 mg, was followed by maintenance of anaesthesia with enflurane in oxygen and nitrous oxide. The surgeon was surprised, at the end of the operation, to find that the repair of the palate had brought the enlarged tonsils into complete approximation in the midline. Indeed, the oral airway was restricted to a small slit above the tracheal tube. Formal adenotonsillectomy is contraindicated, since it removes the site of superior contact of the surgically repaired palate and prevents velopharyngeal closure. This velopharyngeal incompetence significantly impairs normal speech development and cannot be overcome through training or exercises. The surgeon elected to pass a large stitch through the substance of the tonsils and suture them laterally to enlarge the oral airway. It was decided, after discussion between the anaesthetist and surgeon, to leave the tracheal tube in place overnight to allow time for the swelling and operative bleeding to settle. No attempt was made to insert a nasal airway because of the risk of disruption of the surgical repair and haemorrhage. The following day, the child was given halothane anaesthesia to remove the tonsillar sutures and the trachea was extubated under direct vision. The airway, though still restricted, was judged to be adequate and he maintained satisfactory gas exchange whilst breathing humidified oxygen through his mouth until his full recovery.

One should always be careful to examine for tonsillar enlargement in children about to undergo palatal surgery, since recognition of a potential problem is the best way of preventing complications. Alternatives to our management include the elective use of a nasotracheal tube which could be withdrawn postoperatively to provide a nasopharyngeal airway. Surgery could also be postponed until either the tonsils shrink or a limited tonsillectomy has been performed.

Department of Anaesthesia, B.C. SELLICK
St George's Hospital,
Blackshaw Road,
London SW17 OQT

Reference

1. LEE JT, KINGSTON HGG. Airway obstruction due to massive lingual oedema following cleft palate surgery. *Canadian Anaesthetists' Society Journal* 1985; **32**: 265–7.

Anaesthesia in myopathy of carnitine deficiency

The rare association of carnitine deficiency with lipid storage myopathy has recently been described.[1,2]

Carnitine is an enzyme which facilitates oxidation of long chain free fatty acids by promoting their transport into mitochondria. Clinically, two distinct entities are seen:[2] a myopathic form with muscle weakness and a systemic form which additionally is characterised by recurrent hepatic encephalopathy. Most patients die early in life from respiratory insufficiency or from congestive heart failure secondary to cardiomyopathy. Treatment with oral carnitine or high dose steroids may be effective. Anaesthetic experience with this devastating multisystem disease is limited. One reported case has come to our attention.[3] This involved a child with carnitine deficiency who suffered had massive rhabdomyolysis and cardiac arrest following general anaesthesia.

We report an eight-month-old infant with the myopathic form of carnitine deficiency, who underwent general anaesthesia for tracheostomy. Since age 5 months he suffered from recurrent pneumonia, which required repeated and prolonged tracheal intubation because of respiratory insufficiency. Anaesthesia was induced and maintained with 50% nitrous oxide in oxygen and 1–1.5% halothane. Ventilation was assisted manually using the Jackson-Rees modification of the Ayre's T-piece. Muscle relaxants were not used because of their unpredictable action in patients with myopathies. Patients with carnitine deficiency are largely dependent on glucose for energy production, and we therefore administered intravenous 5% dextrose in 0.45% saline continuously throughout the procedure, which lasted 40 minutes. Heart rate remained stable at 120–140 beats/minute, and blood pressure, measured by a Doppler detector, ranged between 80/50 and 60/40 mmHg. Rectal temperature was maintained between 36.4 and 36.2°C. The infant awoke at the end of the procedure whil breathing 100% oxygen and his condition was satisfactory. His postoperative course was uneventful.

In contradistinction to the only previously reported case of general anaesthesia in a patient with carnitine deficiency, which had a disastrous outcome, we have found that the administration of nitrous oxide and oxygen with halothane in this infant was well tolerated.

Department of Anaesthesia, B. BEILIN
PO Box 24035, D. SHULMAN
Hadassah University Hospital, Y. SCHIFFMAN
Mount Scopus,
Jerusalem,
Israel

References

1. DI MAURO S, TREVISAN C, HAYS A. Disorders of lipid metabolism in muscle. *Muscle and Nerve* 1980; **3**: 369–88.
2. RUDOLPH AM. *Pediatrics*. XVII Appleton Century Crofts Norwall, Kentucky; 1982, 1695–6.
3. CORNELIO F, DI DONATO S, TESTA D, MOZA M, GORI G, PULUCHETTI D, RIMOLDI M. 'Carnitine defficient' myopathy and cardiomyopathy with fatal outcome. *Italian Journal of Neurological Sciences* 1980; **1**: 95–100.

Atracurium and McArdle's disease

McArdle's disease, glycogenosis V, is a hereditary myopathy caused by a deficiency of the muscle phosphorylase which converts glycogen to lactate. Glycogen therefore accumulates in the muscles and patients suffer from pain on exercise, relieved by rest. Myoglobinuria may occur after severe exercise and, rarely, this may precipitate renal failure.[1]

A 4-year-old boy (weight 18.2 kg) who had been diagnosed as a probable case of McArdle's disease was presented for adenoidectomy. He had a history of cramp-like pains in his legs on exertion, and recurrent chest infections. On examination he had pseudohypertrophy of the calves, but no other abnormalities. His serum creatine phosphokinase (CPK) was raised at 298 iu/litre (normal 1–130 iu/litre). He was considered too young, as yet, to undergo confirmatory muscle biopsy. His elder sister, aged 10 years, had presented with similar symptoms accompanied by mild pes cavus and clumsiness of gait. Her CPK was 1500 iu/litre. Two other siblings had died, one aged 7 weeks and one aged 5 months, of infective episodes.

In this disease it is recommended that suxamethonium be avoided,[2] because it may cause myoglobinaemia and myoglobinuria with the risk of renal failure. Therefore atracurium was used as the muscle relaxant in this case, since its length of action is suitable for adenoidectomy. Premedication was with trimeprazine tartrate 36 mg orally 2 hours pre-operatively. Anaesthesia was induced with thiopentone 100 mg and atracurium 10 mg was then administered. Following intubation of the trachea, anaesthesia was maintained with nitrous oxide 70% in oxygen and fentanyl 20 μg. Neuromuscular blockade was reversed with neostigmine and atropine at the end of the procedure, 20 minutes later.

Venous blood was taken to monitor serum potassium and CPK immediately after induction, 10 minutes after induction, and the next morning (24 hours later). There was a slight rise in potassium by the end of the procedure, but not to dangerous levels. The CPK tended to fall over the observation period, although all samples were within the normal range. Urine was tested postoperatively and at 24 hours for myoglobinuria. None was found.

Atracurium would therefore seem to be a safe agent to use to produce neuromuscular relaxation for short procedures in a patient with McArdle's disease.

Department of Anaesthetics,
Ysbyty Glan Clwyd,
Bodelwyddan,
Clwyd, LL18 5VJ

A. Rajah
Christine F. Bell

References

1. Katz J, Benumof J, Kadis LB. Anaesthesia and uncommon diseases, 2nd edn. Philadelphia: W.B. Saunders, 1981: 540.
2. Katz J, Benumof J, Kadis LB. Anaesthesia and uncommon diseases, 2nd edn. Philadelphia: W.B. Saunders, 1981: 21–22.

Difficult tracheal intubation

Dr Tomlinson (*Anaesthesia* 1985; **40**: 496–7) uses a 60-cm gum elastic introducer (Eschmann) to intubate tracheas that cannot be seen. There are three ways to tell if the introducer is in the trachea. The tracheal rings may be felt as the introducer slides in. The introducer is held up once small bronchi are reached, whereas if the oesophagus is intubated all 60 cm can be inserted (this idea should be attributed to Professor F. Cheney, University of Washington, Seattle). Thirdly, the patient may cough, if the introducer is in the trachea and anaesthesia is not profound.

Bristol Maternity Hospital,
Southwell Street,
Bristol, BS2 8EG

W.F.S. Sellers
G.W. Jones

Recovery?

Dr R.D. Stark's description of the bullseye walking test, (*Anaesthesia* 1985; **40**: 822), prompts me to suggest that patients might spontaneously generate the information that we really require.

The various anaesthetic mixtures used for patients undergoing termination of pregnancy at Lewisham Hospital on the 09.00 hours list result in some degree of postoperative somnolence. Typically, the patients lunch at 12.30 hours, dress before 14.00 hours and leave by 14.30 hours. If intermittent thiopentone is used these times are extended by up to 2 hours. When propofol was evaluated the patients we complaining that they were hungry at 12.00 hours and were all ready to leave by 13.00 hours!

Patients who spontaneously get up, eat and dress provide the indicator of street fitness that we really need.

Lewisham Hospital,
London, SF13 6LH

J.M. Cundy

Anaesthesia, 1986, Volume 41, pages 94–96

Audiovisual reviews

An introduction to medical statistics 94
Oxford Educational Resources Ltd. (Tapeslide lectures)
CPR for heartsavers 95
Laerdal Medical Limited (VHS Videocassette)
CPR for citizens 95
Laerdal Medical Limited (VHS Videocassette)
ABC of resuscitation 95
Vitalograph Ltd VHS-U-Matic videocassette)
Collapse—A basic guide to first aid 95
Holiday Brothers (Videocassette)
ABC of cardiopulmonary resuscitation 95
Stewart Film Distributors (VHS/Betamax/U-Matic Videocassette or film 16 mm)

An introduction to medical statistics

L.A. GOLDSTONE (*Newcastle University*). Tapeslide lectures. Buy from Oxford Educational Resources Ltd., 197 Botley Road, Oxford, OX2 0HE.

This series of tapeslide lectures is intended to provide an introduction to medical statistics and the first four parts (part two is divided into two lectures) of the series considered in this review develop the subject as far as measures of spread. The series is very suitable for those with no previous knowledge of the subject but the treatment is very thorough and includes relevant topics not usually encountered in introductions to medical statistics. The pace is deliberately slow, and the algebraic content is introduced gradually and clearly with a steady progression from the use of numbers to the use of symbols. The use of statistical tables is explained where appropriate and the use of a calculator with statistics functions is mentioned briefly in some of the lectures. The content of the lectures is well chosen, the only omission being a discussion of the use of percentiles.

Part 1 covers the use of graphs and diagrams to illustrate statistics and includes bar charts, pie diagrams and pictograms. Part 2A includes a description of histograms and proceeds to a detailed discussion of the preparation of histograms from raw data and the problems of labelling. Averages and measures of the centrality of a distribution such as the mean, mode and median are introduced. In part 2B discussion of the uses of histograms is continued. Again, practical problems such as the calculation of the median are discussed in detail. The programme finishes with a description of the calculation and use of the geometric mean. Part 3 describes measures of dispersion such as range, mean absolute deviation, standard deviation and variance. In part 4 coefficient of variation, the normal distribution, standard normal distribution and z values are introduced and the spread of results is discussed. The problem of non-Gaussian distributions is tackled by the use of Tchebbycheff's theorem.

The reviewer does not envy anyone approaching the task of preparing a tapeslide lecture series on statistics. The numerical nature of the subject makes it very difficult to produce interesting slides and this series does have a number of illustrations which consist of lists of perhaps 100 numbers. By the time part 4 is reached it is becoming difficult to concentrate when figures are added together by the lecturer without the results being displayed at the same time on the screen.

There is a tendency to introduce topics in one lecture which are not explained until a later lecture and to re-use slides so that labels are not explained the first time the slide is viewed. The occasional use of a bleep in the middle of a sentence so that the slide changes as the lecturer is speaking is also disconcerting. The rate at which the lecturer speaks in the first lecture or two is rather slow, although this does speed up in later lectures.

In conclusion, although the procedures have not managed to overcome all the problems of presenting a subject such as this in the medium of tapeslide, the content of this series of programmes is one of the best and most relevant introductions to medical statistics that the reviewer has seen.

P.D. DAVIS

CPR for heartsavers

By Laerdal Medical Ltd., VHS Videocassette. Colour. Buy from Laerdal Medical Ltd., 2 Vinson Close, Orpington, Kent. 19 min. 1981. (£50.00 + VAT).

CPR for citizens

By Laerdal Medical Ltd., VHS Videocassette. Colour. Buy from Laerdal Medical Ltd., 2 Vinson Close, Orpington, Kent. 29 min. 1981. (£75.00 + VAT).

These American presentations, available as video cassettes, are intended as educational films for the general public. Because their contents overlap, they are reviewed together.

CPR for heartsavers has a British commentary throughout most of the presentation. It deals principally with myocardial infarction, and opens with a view of a beating heart. The causes of cardiac arrest are considered, and risk factors associated with myocardial infarction, together with preventive measures, are discussed. The symptoms and signs resulting from acute myocardial infarction are described. There is an explanation of the term 'CPR', and the individual components of Airway, Breathing and Circulation are emphasised. Airway control is demonstrated using a model, and mouth-to-mouth and mouth-to-nose ventilation explained. To illustrate the effects of artificial ventilation, there is a brief view of cadaveric lungs inflating. Techniques of external cardiac massage are demonstrated, predominantly with one rescuer. Correct and incorrect methods are contrasted. The film ends with a slightly forced, and very American, dramatisation of cardiac arrest and resuscitation.

CPR for citizens is an expanded and more broadly based version of the same film. The subject matter is extended to include accidents as well as myocardial infarction. The importance of cerebral oxygen requirements is emphasised. Combined cardiorespiratory resuscitation with two rescuers is dealt with more fully and the management of cardiac arrest in infants and children is described. A separate section deals with airway obstruction by a foreign body in conscious and unconscious patients. There is a very clear commentary by Orson Welles. The film concludes with another dramatised resuscitation.

These films are clear and accurate, although allowance has to be made for their American origins.

ABC of resuscitation

By Vitalograph Ltd., VHS/U-Matic Videocassette. Colour. Buy from Vitalograph Ltd., Maids Moreton House, Buckingham, MK18 1SW. 20 min. 1984. (£46.57 inc VAT).

This excellent video presentation deals with the basic steps of resuscitation of victims of accidents or cardiac arrest. The presentation begins with four brief dramatised reconstructions depicting electrocution, a road traffic accident, a drowning incident and a myocardial infarction. Following a brief introduction from a Bristol anaesthetist well known for his interest in emergency medicine, the first aid management of each of the four victims is discussed. The importance of avoiding further injury, either to the victim or the rescuer, and the need to obtain skilled assistance are emphasised. By dealing with the resuscitation of each victim in turn, the practical aspects of the recovery position, airway control, artificial ventilation and external cardiac are taught in a logical progression. Airway control is demonstrated using an effective graphic technique. Mouth-to-mouth ventilation and cardiac massage are explained clearly. There is a good dramatised simulation of airway obstruction by a foreign body.

Although relatively short, the presentation is comprehensive and concise. It uses the medium of television of television graphics and freeze-frame effectively. The commentator emphasises that the presentation is intended to complement, not to replace, a resuscitation course and experience of the practical procedures using a manikin.

Collapse—A basic guide to first aid

A. Redmond and D. Edwards (*Stockport Infirmary*). Videocassette. Colour. Buy from Holiday Brothers (Audio and Video Ltd.), 172 Finney Lane, Heald Green, Cheadle, Cheshire, SK8 3PU. 30 min. 1985. (£19.95 inc VAT).

This resuscitation video is comprehensive in that it describes cardiopulmonary resuscitation in adults and children, the treatment of a choking victim, and the management of a patient having an epileptic seizure. However, there is a paucity of visual demonstrations of the mechanisms of action of the techniques described. Some of the techniques which are demonstrated are inaccurate, e.g. external cardiac massage is shown at a rate of approximately 20/minute. The sequence of the presentation could have been improved, and the standard of acting is poor and unconvincing.

ABC of cardiopulmonary resuscitation

Stewart Film Distributors, VHS/Betamax/U-Matic Videocassette or film 16 mm. Colour. Buy from Stewart Film Distributors Ltd., 107–115 Long Acre, London, WC2E 9NU. 13 min. 1983. (Videocassette £200.00 + VAT).

This is an excellent presentation, which is clear, dogmatic and concise. The necessity for a continuing supply of oxygen to the brain and heart is emphasised, and causes of hypoxaemia described. Cardiopulmonary resuscitation is explained and demonstrated extremely well, and the graphical illustrations are of a high quality. There are good dramatisations of drowning and smoke inhalation, and there is a continual emphasis of the importance of rapid initiation of treatment and the continuation of treatment until professional help arrives.

In this reviewer's opinion, the best presentations of the five are *ABC of cardiopulmonary resuscitation*

Macintosh, Mushin and Epstein: Physics for the Anaesthetist

W.W. Mushin and **P.L. Jones.**
Fourth Edition, Early 1986. 640 pages,
350 illustrations. About £25.00

Patient-Controlled Analgesia

Edited by **M. Harmer, M. Rosen** and
M.D. Vickers. 1985. 224 pages,
50 illustrations. £18.00 *Blackwell*

Guidelines in Clinical Anaesthesia

P. Hutton and **Griselda Cooper.** 1985.
416 pages, 54 illustrations. £19.50

Ventilation/Blood Flow and Gas Exchange

J.B. West. Fourth Edition, 1985. 128 pages,
57 illustrations. Paper, £6.50

Perinatal Anesthesia

Contemporary Issues in Fetal and Neonatal Medicine, Volume 1

Edited by
J.W. Scanlon.
352 pages,
22 illustrations.
About
£25.00

New books from
Blackwell Scientific Publications Ltd
Osney Mead
Oxford
OX2
0EL

THE ASSOCIATION OF ANAESTHETISTS
OF GREAT BRITAIN AND IRELAND

Nine Bedford Square

A CENTRE FOR ANAESTHESIA

The Association has now moved to
Nine Bedford Square, London WC1B 3RA.

Telephone: 01 631 1650

G&S GRUNE & STRATTON

An invaluable and practical sourcebook!

REGIONAL ANESTHESIA:

Techniques and Clinical Applications

HAROLD CARRON, M.D., GREGG A. KORBON, M.D.,
and JOHN C. ROWLINGSON, M.D.

Regional Anesthesia: Techniques and Clinical Applications is designed as a pragmatic reference for all physicians and other professionals who use regional anesthesia in their practice. Written by well-known teachers in the field, the text provides clearly defined guidelines on anatomical considerations, concise descriptions of surface landmarks, and techniques for performing regional anesthetic procedures.

The book is divided into six sections dealing sequentially with plexus blocks, the neural axis, peripheral nerves, pain management, and concludes with techniques enhancing the success of blocks and a discussion of systemic and neurologic complications of block procedures. A guest chapter by C.A. DiFazio, M.D., Ph.D., discusses the pharmacologic considerations in choice and dosage of local anesthetics. Complications incident upon specific blocks are described briefly at the end of each chapter.

This work is further enhanced by its profusely illustrated text, including 16 color illustrations. Photographs of living subjects depict superficial anatomical landmarks and are accompanied by cut-away drawings illustrating the relationship of landmarks to nerves to be blocked.

CONTENTS: *Cosmo A. DiFazio, M.D., Ph.D.*, Introduction: **Pharmacology of Local Anesthetics and Choice of Agents. Plexus Blocks:** Cervical Plexus Block. Brachial Plexus Block. Lumbar Plexus Block. **Neural Axis Blocks:** Subarachnoid Block. Epidural Block. **Peripheral Blocks:** Head and Neck Block. Intercostal Block. Abdominal Blocks. Upper Extremity Blocks. Lower Extremity Blocks. Miscellaneous Nerve Blocks. **Pain Blocks:** Sympathetic Blocks. Special Procedures. Neurolytic Blocks. **Enhancing Regional Procedures:** Enhancing Regional Techniques. Needles. Nerve Stimulators. **Complications:** Systemic Complications. Neurologic Complications. Technical Complications. Suggested Readings. Subject Index.

1984, 208 pp., 16 color illustrations, £34.50/$39.50
ISBN: 0-8089-1654-8, Order Code: 790797

G&S GRUNE & STRATTON, INC. *(Harcourt Brace Jovanovich, Publishers)*
Attn: Promotion Dept., Orlando, FL 32887-0018, U.S.A.

Please enter the following order:

ORDER CODE	AUTHOR/TITLE/VOLUME

☐ Please check if you are a Grune & Stratton or Academic Press author.
U.S. Customers: Payment will be refunded of titles on which shipment is not possible within 120 days.
Prices are in £ Sterling and are subject to change without notice.

Name ____________________ (Please Print)
Address ____________________
City ________ State ________ Zip ________
Signature ____________________

SAVE: Prepay or use your credit card and we pay postage and handling.
Please check one box
☐ Payment Enclosed (add applicable sales tax)
☐ American Express ☐ Diners Club
☐ MasterCard ☐ Visa ☐ Bill me
Charge Card # ________
Expiration Date (mo/yr) ________
84124

Grune & Stratton, Inc.
(Harcourt Brace Jovanovich, Publishers)
Orlando, Florida 32887

Orlando San Diego New York London Toronto Montreal Sydney Tokyo

For Fastest Service *CALL TOLL FREE 1-800-321-5068.* To Place An Order From Florida, Hawaii, Or Alaska *CALL 1-305-345-4100.* In The U.K. *CALL (01) 300-0155.* Credit Card Orders Only. Send payment with order and save postage and handling. Prices are subject to change without notice.

Anaesthesia, 1986, Volume 41, pages 97–105

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for July 1985. The journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Abdominal surgery

Proliferative and morphologic changes in rat colon following bypass surgery. BARKLA, D.H. TUTTON, P.J.M. *American Journal of Pathology* 1985; **119:** 402.

Effect of diverting colostomy on breaking strength of anastamoses after resection of the left side of the colon. Studies in the rat. BLOMQUIST, P., JIBORN, H., ZEDERFELDT, B. *American Journal of Surgery* 1985; **149:** 712.

Respiratory performance after upper abdominal surgery. A comparison of pain relief with intercostal blocks and centrally acting analgesics. ENGBERG G. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 427.

Factors influencing the respiratory capacity after upper abdominal surgery. ENGBERG, G. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 434.

Effects of beta-adrenoceptor stimulation on rectosigmoid motility in man. LYRENAS, E., ABRAHAMSSON, H. DOTEVALL, G. *Digestive Diseases and Sciences* 1985; **30:** 536.

Perioperative allogenic blood transfusions: survival in patients with resected carcinomas of the colon and rectum. NATHANSON, S.D., TILLEY, B.C. *et al.* *Archives of Surgery* 1985; **120:** 734.

Extracellular fluid deficit following operation and its correction with ringer's lactate: a reassessment. ROBERTS, J.P. *et al.* *Annals of Surgery* 1985; **202:** 1.

Influence of fentanyl and morphine on intestinal circulation. TVERSKOY, M., GELMAN, S. *et al.* *Anesthesia and Analgesia* 1985; **64:** 577.

Pharmacology

Adrenergic drugs and their antagonists

Beta-adrenergic blockers in cirrhosis. Leading article. *Lancet* 1985; **1:** 1372.

Mechanisms involved in alpha-adrenergic phenomena. EXTON, J.H. *American Journal of Physiology* 1985; **248:** E633.

Control of myocardial catecholamine release during acute ischemia. FORFAR, J.C., RUSSELL, D.C., RIEMERSMA, R.A. *Journal of Cardiovascular Pharmacology* 1985; **7:** S33.

Selected aspects of presynaptic modulation of noradrenaline release from the heart. FUDER, H. *Journal of Cardiovascular Pharmacology* 1985; **7:** S2.

Effects of propranolol on hepatic haemodynamics in the cirrhotic and non-cirrhotic rat. JENKINS, S.A., BAXTER, J.N. *et al.* *British Journal of Surgery* 1985; **72:** 354.

Relationship between dose, blood level and haemodynamic response in patients with cirrhosis receiving propranolol. JIRON, M.I., DELHOTAL, B., LEBREC, D. *European Journal of Clinical Pharmacology* 1985; **28:** 353.

Pulmonary ventilation in long-term beta-adrenergic blockade after myocardial infarction. JOHANSEN, S. *European Journal of Clinical Pharmacology* 1985; **28:** 23.

Theophylline toxicity and the beta-adrenergic system. KEARNY, T.E., MANOGUERRA, A.S. *et al.* *Annals of Internal Medicine* 1985; **102:** 766.

Prazosin does not alter levels of plasma lipids, glucose and insulin. PLOUIN, P.F. *Journal of Cardiovascular Pharmacology* 1985; **7:** 516.

The distribution of catecholamines between platelets and plasma in normal human subjects. SMITH, C.C.T., CURTIS, L.D. *et al.* *Clinical Science* 1985; **69:** 1.

Adrenergic interactions in smooth muscle contractility. TRIGGLE, C.R. *Calcium and Contractility Smooth Muscle Contemporary Biomedicine Humana Press Inc* (Clifton) 1985: 327.

Anaesthetic agents

The effect of atropine and vagal stimulation on the

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London, WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. An exact copy of the monthly section or various cumulative classifications of the Anaesthetic Literature published in the Journal can be obtained on application to him. References from January 1984 have been entered on data base and search facilities are also available. All communications about this matter should be addressed to Dr Kaufman please.

release of neurotensin-like immunoreactivity in man (RPT 00358). Eaves, E.R. *et al. Regulatory Peptides* 1985; **11:** 1.

Cardiovascular effects of enflurane and asphyxia during long-term beta-adrenoceptor blockade. Henriksson, B.A., Biber, B. *et al. Acta Anaesthesiologica Scandinavica* 1985; **29:** 363.

The effect of increasing age on thiopental disposition and anaesthetic requirement. Homer, T.D., Stanski, D.R. *Anesthesiology* 1985; **62:** 714.

Prediction of thiopental induction dose based on caffeine volume. Inchiosa, M.A., Schmahai, T.J. *et al. Journal of Clinical Pharmacology* 1985; **25:** 281.

Ventilatory responses to acute metabolic acidemia in humans awake, sedated and anesthetized with halothane. Knill, R.L., Clement, J.L. *Anesthesiology* 1985; **62:** 745.

Isoflurane as a routine anaesthetic in general surgical practice. Nunn, J.F. *British Journal of Anaesthesia* 1985; **57:** 461.

Kinetics of ketamine and its metabolites in rabbits with normal and impaired renal function. Pedraz, J.L., Lanao, J.M. *et al. European Journal of Drug Metabolism and Pharmacokinetics* 1985; **10:** 33.

Sex differences in halothane metabolism and hepatotoxicity in a rat model. Plummer, J.L., Hall, P.D. *et al. Anesthesia and Analgesia* 1985; **64:** 563.

Relationships between the pharmacokinetics of carbon tetrachloride conversion to carbon and chloroform and liver injury. Reynolds, E.S., Treinen, R.J. *et al. Archives of Toxicology* 1984; **7:** 303.

Different pathways of chloroform metabolism. Testai, E., Vittozzi, L. *Archives of Toxicology* 1984; **7:** 278.

Analgesic agents

Use of alfentanil in short anaesthetic procedures. Collins, K.M., Plantevin, O.M. *Journal of the Royal Society of Medicine* 1985; **78:** 456.

CSF and plasma pharmacokinetics of intramuscular morphine. Nordberg, G., Borg, L. *et al. European Journal of Clinical Pharmacology* 1985; **27:** 677.

Influence of naloxone on the antinociceptive effects of some antidepressant drugs. Reichenberg, K., Caillard-Plaza, G. *et al. Archives Internationales de Pharmacodynamie et de Therapie* 1985; **275:** 78.

GABA in morphine analgesia. Sivam, S.P., Ho, I.K. *Life Sciences* 1985; **37:** 199.

Changes in succinic dehydrogenase activity in the central nervous system of mice during morphine dependence development. Sood, P.P., Mohanakumar, K.P. *Clinical Physiology and Biochemistry* 1985; **3:** 193.

Long-term changes in self-stimulation threshold by repeated morphine and naloxone treatment. Vanwolfswinkel, L., Seifert, W.F., Vanree, J.M. *Life Sciences* 1985; **37:** 169.

Muscle relaxants

Fade characteristics and onset times following administration of pancuronium, tubocurarine and a mixture of both agents. Cashman, J.N., Jones, R.M., Vella, L.M. *British Journal of Anaesthesia* 1985; **57:** 488.

4-aminopyridine—an anticurare and reawakening drug. Malizia, E., Nicolai, P. *et al. Archives of Toxicology* 1984; **7:** 468.

The use of physostigmine in heroin overdose. Ruprecht, J., Dworacek, B. *et al. Archives of Toxicology* 1984; **7:** 467.

Vasodilators. Stricker, B.H.C., Spoelstra, P. *Drug-Induced Hepatic Injury* 1985; **1:** 286.

Other drugs

Ventilatory effects of domperidone, a new dopamine antagonist, in anaesthetized rabbits. Delpierre, S., Peyrot, J. *et al. Archives Internationales de Pharmacodynamie et de Therapie* 1985; **275:** 47.

Active drug metabolites: an overview. Garattini, S. *Clinical Pharmacokinetics* 1985; **10:** 216.

Aminoglycoside antibiotics—a study of their neurotoxic effects at peripheral nerve fibres. Mitolochieppa, D., Carratu, M.R. *Archives of Toxicology* 1984; **7:** 464.

Apparatus

Transcutaneous temporary pacing in the operating room. Berliner, D., Okun, M. *et al. Journal of the American Medical Association* 1985; **254:** 84.

Intracuff pressures in endotracheal and tracheostomy tubes. Bernhard, W.N., Yost, L. *et al. Chest* 1985; **87:** 720.

Elective percutaneous dilatational tracheostomy; a new simple bedside procedure. Ciaglia, P., Fisching, R., Syniec, C. *Chest* 1985; **87:** 715.

Tracheal intubation kit for resuscitation. Conacher, I.D. *Lancet* 1985; **1:** 1424.

Automatic blood pressure monitors. A clinical evaluation of five models in adults. Johnson, C.J.H., Kerr, J.H. *Anaesthesia* 1985; **40:** 471.

The usefulness of preoperative laboratory screening. Kaplan, E.B., Sheiner, L.B. *et al. Journal of the American Medical Association* 1985; **253:** 3576.

The case for continued scrutiny of catheterization-related complications. Kron, J. *Chest* 1985; **87:** 707.

Tracheal tube cuff pressures. The effects of different gas mixtures. Raeder, J.C., Borchgrevink, P.C. *et al. Anaesthesia* 1985; **40:** 444.

Self-monitoring of the blood glucose level: potential sources of inaccuracy. Rasaiah, B. *Canadian Medical Association Journal* 1985; **132:** 1357.

Complications

Acute gastric dilatation following upper gastrointestinal endoscopy. Ahmed, M.E.K., Ahmed, M.E. *et al. Endoscopy* 1985; **17:** 117.

Pancreatitis after cardiac and cardiopulmonary transplantation. Aziz, S., Bergdahl, L. *et al. Surgery* 1985; **97:** 653.

Laryngeal injury in a dog model of prolonged endotracheal intubation. Bishop, M.J., Hibbard, A.J. *et al. Anesthesiology* 1985; **62:** 770.

Cardiac arrest: a follow-up. Davis, L. *Medical Journal of Australia* 1985; **142:** 671.

Recurrent cardiac arrest. Fagan, E.T. *Medical Journal of Australia* 1985; **142:** 667.

Amiodarone-induced hypothyroidism. Hawthorne, G.C., Campbell, N.P.S. *et al. Archives of Internal Medicine* 1985; **145:** 1016.

Acute brain edema due to water loading in young women. Kott, E., Marcus, Y. *European Neurology* 1985; **24:** 221.

Acute renal failure in the cardiovascular surgical patient. Kron, I.L., Joob, A.W., Van Meter, C. *Annals of Thoracic Surgery* 1985; **39:** 590.

Severe neutropenia associated with procainamide: comparison of sustained release and conventional preparations. Meyers, D.G., Gonzalez, E.R. *et al. American Heart Journal* 1985; **109:** 1393.

Thrombocytopenic purpura in narcotics addicts. Savona, S., Nardi, M.A. *et al. Annals of Internal Medicine* 1985; **102:** 737.

Pentazocine-induced agranulocytosis. Sheehan, M. *et al. Canadian Medical Association Journal* 1985; **132:** 1401.

Seizures due to theophylline overdose. Singer, E.P., Kolischenko, A. *Chest* 1985; **87:** 755.

Patterns of drug-induced hepatic injury. Stricker, B.H.C., Spoelstra, P. *Drug-Induced Hepatic Injury* 1985; **1:** 1.

Mechanisms of drug-induced hepatic injury. Stricker, B.H.C., Spoelstra, P. *Drug-Induced Hepatic Injury* 1985; **1:** 11.

Diagnosis and analysis of drug-induced hepatic injury. Stricker, B.H.C., Spoelstra, P. *Drug-Induced Hepatic Injury* 1985; **1:** 21.

Anesthetics. Stricker, B.H.C., Spoelstra, P. *Drug-Induced Hepatic Injury* 1985; **1:** 33.

Intramuscular injections and muscle damage—effects of concentration, volume, injection speed and vehicle. Svendsen, O., Blom, L. *Archives of Toxicology* 1984; **7:** 472.

Cyanide-induced parkinsonism—a clinicopathologic report. Uitti, R.J., Rajput, A.H. *et al. Neurology* 1985; **35:** 921.

A study of post-intubation laryngeal dysfunction. Whited, R.E. *The Laryngoscope* 1985; **95:** 727.

General anaesthetic procedures

Cardiac rate and rhythm during anaesthesia for dental extraction—a comparison of halothane, enflurane and isoflurane. Casson, W.R., Jones, R.M. *British Journal of Anaesthesia* 1985; **57:** 476.

Circulatory responses to thiopentone and tracheal intubation in patients with coronary artery disease—effects of pretreatment with labetalol. Fischler, M., Dubois, C. *et al. British Journal of Anaesthesia* 1985; **57:** 493.

The effect of diazepam pretreatment on the succinylcholine-induced rise in intraocular pressure. Fjeldborg, P., Hecht, P.S. *et al. Acta Anaesthesiologica Scandinavica* 1985; **29:** 415.

Anesthesia with ketanserin and alfentanil in the elderly. Helmers, J.H., Adam, A.A. *et al. Current Therapeutic Research* 1985; **37:** 1075.

Smoking before surgery: the case for stopping. Jones, R.M. *British Medical Journal* 1985; **290:** 1763.

Comparison between complications of cataract surgery following local anaesthesia with short stay and general anaesthesia with a 5-day hospitalization. Vernon, S.A., Cheng, H. *British Journal of Ophthalmology* 1985; **69:** 360.

General interest

Erroneous diagnosis of phaeochromocytoma in hypertensive patients on labetalol. Bouloux, P-M. *et al. Journal of the Royal Society of Medicine* 1985; **78:** 588.

Potassium depletion myopathy: a clinical and morphological study of six cases. Comi, G., Testa, D. *et al. Muscle and Nerve* 1985; **8:** 17.

Clonidine-suppression test in epinephrine secreting pheochromocytoma: report of a case. Dupont, A.G., Vanderniepen, P. *et al. Journal of Endocrinological Investigation* 1985; **8:** 153.

Prolonged surgical intensive care: a useful allocation of medical resources. Madoff, R.D., Sharpe, S.M. *et al. Archives of Surgery* 1985; **120:** 698.

Increase in radiosensitivity of lung micrometastases by hyperbaric oxygen. Milas, L., Hunter, N.M. *et al. Clinical and Experimental Metastasis* 1985; **3:** 21.

Tetrodotoxin derivatives in puffer fish. Nakamura, M., Yasumoto, T. *Toxicon* 1985; **23:** 271.

Efficacy of opical nitroglycerin for random-pattern skin-flap salvage. Nichter, L.S., Sobieski, M.W., Edgerton, M. *Plastic and Reconstructive Surgery* 1985; **75:** 847.

A sleep-inducing peptide from conus-geographus venom. Olivera, B.M. *et al. Toxicon* 1985; **23:** 277.

Enkephalins in pheochromocytoma: studies in a rat model. Palmer, R.J., Mosley, C., O'Connor, D.T. *Clinical and Experimental Hypertension: Part A. Theory & Practice* 1985; **7:** 483.

Carcinoid tumors of the colon: a study of 72 patients. Rosenberg, J.M., Welch, J.P. *American Journal of Surgery* 1985; **149:** 775.

Dental factors in infective endocarditis. Seldin, E.B. *Circulation* 1985; **71:** 1093.

Hypercalcemia in pheochromocytoma: evidence for a novel mechanism. STEWART, A.F., HOECKER, J.L. *et al. Annals of Internal Medicine* 1985; **102:** 776.

Spinal and epidural analgesia

Safety and efficacy of epinephrine added to bupivacaine for lumbar epidural analgesia in obstetrics. ABBOUD, T.K., SHEIK-OL-ESLAM, A. *et al. Anesthesia and Analgesia* 1985; **64:** 585.

Distribution of local anesthetic solutions within the subarachnoid space. GREENE, N.M. *Anesthesia and Analgesia* 1985; **64:** 715.

Spinal opioids

Increased dynorphin immunoreactivity in spinal cord after traumatic injury (RPT 00362). FADEN, A.I. *Regulatory Peptides* 1985; **11:** 35.

The cardiovascular actions of morphine and the endogenous opioid peptides. JOHNSON, M.W., MITCH, W.E., WILCOX, C.S. *Progress in Cardiovascular Diseases* 1985; **27:** 435.

Endogenous opioid activity in clinical hemorrhagic shock. SHATNEY, C.H., COHEN, R.M. *et al. Surgery Gynecology & Obstetrics* 1985; **160:** 547.

Endogenous opioid peptides in the regulation of arterial blood pressure. VANLOON, G.R. *Hypertension and the Brain* 1984; New York: 127.

Direct opioid application to peripheral nerves does not alter compound action potentials. YUGE, O. *et al. Anesthesia and Analgesia* 1985; **64:** 677.

Obstetric anaesthesia and analgesia

Minireview: pregnancy and diabetes: the maternal response. BENDER, H.S., CHICKERING, W.R. *Life Sciences* 1985; **37:** 1.

Hemodynamic observations in severe pre-eclampsia complicated by pulmonary edema. BENEDETTI, T.J., KATES, R., WILLIAMS, V. *American Journal of Obstetrics and Gynecology* 1985; **152:** 330.

Respiratory morbidity benefit of awaiting onset of labor after elective cesarean section. COHEN, M., CARSON, B.S. *Obstetrics and Gynecology* 1985; **65:** 818.

Problems associated with epidural anesthesia in obstetrics. CORKE, B.C., SPIELMAN, F.J. *Obstetrics and Gynecology* 1985; **65:** 837.

Maternal and neonatal responses related to the volatile agent used to maintain anaesthesia at Caesarean section. CRAWFORD, J.S., LEWIS, M., DAVIES, P. *British Journal of Anaesthesia* 1985; **57:** 482.

The effects of naloxone associated with the intrathecal use of morphine in labor. DAILY, P.A. *et al. Anesthesia and Analgesia* 1985; **64:** 658.

Central opioid receptor activity in patients affected by puerperal, idiopathic and tumoral hyperprolactinemia. DE LEO, V., PETRAGLIA, F. *et al. Gynecologic and Obstetric Investigation* 1985; **19:** 160.

Effects of maternal oxygen administration on fetal oxygenation during reductions in umbilical blood flow in fetal lambs. EDELSTONE, D.I., PETICCA, B.B., GOLDBLUM, L. *American Journal of Obstetrics and Gynecology* 1985; **152:** 351.

Elimination kinetics of thiopentone in mothers and their newborn infants. GASPARI, E., MARRARO, G. *European Journal of Clinical Pharmacology* 1985; **28:** 321.

Lack of beta-endorphin plasma level rise in oxytocin-induced labor. GENAZZANI, A.R., PETRAGLIA, F. *et al. Gynecologic and Obstetric Investigation* 1985; **19:** 130.

Maternal and fetal plasma concentrations of ritodrine. GROSS, T.L., KUHNERT, B.R. *et al. Obstetrics and Gynecology* 1985; **65:** 793.

Plasma protein binding of ritodrine at parturition and in nonpregnant women. GROSS, A.S., BROWN, K.F. *European Journal of Clinical Pharmacology* 1985; **28:** 479.

Effect of treatment with sodium valproate on plasma adrenocorticotropic hormone and cortisol concentrations in pregnancy. HATJIS, C.G., ROSE, J.C. *et al. American Journal of Obstetrics and Gynecology* 1985; **152:** 315.

Current concepts: postpartum renal failure. HAYSLETT, J.P. *New England Journal of Medicine* 1985; **312:** 1556.

Continuous long-term intravenous beta-sympathomimetic tocolysis. HILL, W.C., KATZ, M. *et al. American Journal of Obstetrics and Gynecology* 1985; **152:** 271.

On the decrease of glucose tolerance in pregnancy: studies of gastro–entero–pancreatic hormones and cortisol. HORNNES, P.J. *Danish Medical Bulletin* 1985; **32:** 79.

Blood velocities in the uterine artery in humans during labour. JANBU, T., KOSS, T. *et al. Acta Physiological Scandinavica* 1985; **124:** 153.

Oxytocin reduces intravenous heroin self-administration in heroin-tolerant rats. KOVACS, G.L., BORTHAISER, Z., TELEGDY, G. *Life Sciences* 1985; **37:** 17.

Analgesia and maternal side effects of pudendal block at delivery. A comparison of three local anesthetics. LANGHOFF-ROOS, J., LINDMARK, G. *Acta Obstetricia et Gynecologica Scandinavica* 1985; **64:** 269.

Self-administered isoflurane in labour. A comparative study with Entonox. MCLEOD, D.D., RAMAYYA, G.P., TUNSTALL, M.E. *Anaesthesia* 1985; **40:** 424.

Clinical pharmacokinetics in pregnancy and perinatology. 1. Placental transfer and fetal side effects of local anaesthetic agents. NAU, H. *Developmental Pharmacology and Therapeutics* 1985; **8:** 149.

Amiodarone in pregnancy. PENN, I.M. *et al. American Journal of Cardiology* 1985; **56:** 196.

Plasma bupivacaine levels associated with extradural anaesthesia for Caesarean section. THOMPSON, E.M., WILSON, C.M. *et al. Anaesthesia* 1985; **40:** 427.

Preeclampsia: an imbalance in placental prostacyclin and thromboxane production. Walsh, S.W. *American Journal of Obstetrics and Gynecology* 1985; **152:** 335.

Paediatric anaesthesia and intensive care

Preterm infants: ventilation and P_{100} changes with CO_2 and inspiratory resistive loading. Duara, S., Abbasi, S. *et al. Journal of Applied Physiology* 1985; **58:** 1982.

Inspiratory force reserve of the respiratory muscles in children with chronic obstructive pulmonary disease. Gaultier, C. *et al. American Review of Respiratory Disease* 1985; **131:** 811.

Ventilatory interaction between oxygen and carbon dioxide in the preterm primate. Guthrie, R.D., Lafranboise, W.A. *et al. Pediatric Research* 1985; **19:** 528.

Defects of metabolism of fatty acids in the sudden infant death syndrome. Howat, A.J., Benett, M.J. *et al. British Medical Journal* 1985; **290:** 1771.

The relationship between perinatal hypoxia and newborn encephalopathy. Low, J.A., Galbraith, R.S. *et al. American Journal of Obstetrics and Gynecology* 1985; **152:** 256.

Maintenance of upper airway patency. Mathew, O.P. *Journal of Pediatrics* 1985; **106:** 863.

Variation in morphine pharmacokinetics in children with cancer. Nahata, M.C., Miser, A.W. *et al. Developmental Pharmacology and Therapeutics* 1985; **8:** 182.

Alteration of arterial gas composition by positive pressure ventilation in the unanaesthetized fetal lamb *in utero*. Willis, D.M. *et al. Biology of the Neonate* 1985; **47:** 295.

Total parenteral nutrition in children. Zlotkin, S.H., Stallings, V.A., Pencharz, P.B. *Pediatric Clinics of North America* 1985; **32:** 381.

Physiology

Cardiovascular system

Cardiorespiratory patterns in severe delirium tremens. Abraham, E., Shoemaker, W.C., McCartney, S. *Archives of Internal Medicine* 1985; **145:** 1057.

Blood pressure responses to ACTH and adrenaline infusions in dogs. Anderson, W.P., Ramsey, D.E. *Clinical and Experimental Hypertension: Part A. Theory and Practice* 1985; **7:** 525.

Cardiovascular adrenoceptor balance during haemorrhagic hypotension and shock. Bond, R.F., Johnson, G. *Circulatory Shock* 1985; **16:** 155.

Changes in ambient temperature alter the blood pressure response to endotoxin and the effectiveness of naloxone. Chen, C.H., O'Leary, E.L. *et al. Circulatory Shock* 1985; **16:** 185.

The influence of naloxone on regional hemodynamics in hemorrhaged rats. Coates, D.P., Seyde, W.C. *et al. Circulatory Shock* 1985; **16:** 173.

Primary pulmonary hypertension: current status. Edwards, W.D. *Modern Concepts of Cardiovascular Disease* 1985; **54:** 29.

Ca-pumps in smooth muscle: one in plasma membrane and another in endoplasmic reticulum. Grover, A.K. *Cell Calcium* 1985; **6:** 227.

The effect of cardiac hypertrophy on the coronary collateral circulation. Harrison, D.G., Barnes, D.H. *et al. Circulation* 1985; **71:** 1135.

Fluid loading increases oxygen consumption in septic patients with lactic acidosis. Haupt, M.T. *et al. American Review of Respiratory Disease* 1985; **131:** 912.

Regulation of muscle blood flow. Hudlicka, O. *Clinical Physiology* 1985; **5:** 201.

The pharmacology of central adrenergic mechanisms for blood pressure control. Kobinger, W. In: *Hypertension and the Brain* 1984; Ed. G.P. Guthrie, T.A. Kotchen: 123.

Role of the autonomic nervous system in mediating the response to naloxone in canine hemorrhagic shock. Lechner, R.B., Gurll, N.R., Reynolds, D.G. *Circulatory Shock* 1985; **16:** 279.

Jugular venous pressure—a re-appraisal. Mittal, S.R. *International Journal of Cardiology* 1985; **8:** 109.

Creatine kinase release after successful percutaneous transluminal coronary angioplasty. Oh, J.K., Shub, C. *et al. American Heart Journal* 1985; **109:** 1225.

Development of myocardial dysfunction in endotoxin shock. Parker, J.L., Adams, H.R. *American Journal of Physiology* 1985; **248:** H818.

The hypercoagulable states. Schafer, A.I. *Annals of Internal Medicine* 1985; **102:** 814.

Late estimation of myocardial infarct size by total creatine kinase nomogram. Shibata, T., Hashimoto, H. *et al. American Heart Journal* 1985; **109:** 1238.

Physiological effects of pH changes on colloid osmotic pressures. Will, B.R., Brace, R.A. *American Journal of Physiology* 1985; **248:** H890.

Enzymatic assessment of myocardial necrosis after cardiac surgery: differentiation from skeletal muscle damage, hemolysis and liver injury. Willems, G.M., Van der Veen, F.H. *et al. American Heart Journal* 1985; **109:** 1243.

Cerebral blood flow regulation in normotension and hypertension. Winn, H.R., Haley, E.C., Berne, R.M. In: *Hypertension and the Brain* 1984; Ed. G.P. Guthrie, T.A. Kotchen: 157.

Cardiovascular system

Treatment and medication

Effects of K^+ on the interaction between cardiac glycosides and $Na.K^-$ ATPase. Akera, T., Ng, Y.C. *et al. European Journal of Pharmacology* 1985; **111:** 147.

Sickle-cell membrane-bound ATPase activation by a novel antisickling agent. Bewaji, C.O., Olorunsogo, O.O., Bababunmi, E.A. *Cell Calcium* 1985; **6:** 237.

Atenolol inhibits in elimination of disopyramide. Bonde, J., Bodtker, S. *et al. European Journal of Clinical Pharmacology* 1985; **28:** 41.

Kinetics of disopyramide after intravenous infusion to patients with myocardial infarction and heart failure. Bonde, J., Helle, R.A. *et al. Acta Pharmacologica et Toxicologica* 1985; **56:** 278.

Verapamil improves cardiac function and increases survival in canine *E. coli* endotoxin shock. Bosson, S., Kuenzig, M. Schwartz, S.I. *Circulatory Shock* 1985; **16:** 307.

Clinical usefulness of flecainide acetate in the treatment of paroxysmal supraventricular arrhythmias. Camm, A.J., Hellestrand, K.J. *Drugs* 1985; **29:** Suppl 4: 7.

Naloxone versus placebo in treatment of septic shock. Demaria, A., Craven, D.E. *et al. Lancet* 1985; **1:** 1363.

Rapid restoration of red blood cell mass in severely anemic surgical patients who refuse transfusion. Dudrick, S.J., O'Donnell, J.J. *et al. Archives of Surgery* 1985; **120:** 721.

Effect of captopril and hydrochloronthiazide on the response to pressor agents in hypertensives. Fruncillo, R.J., Rotmensch, H.H. *et al. European Journal of Clinical Pharmacology* 1985; **28:** 5.

Half-life of digoxin in myocardium after stopping maintenance treatment. Griffiths, B.E., Buss, D. *et al. Journal of Cardiovascular Pharmacology* 1985; **7:** 604.

Improved myocardial recovery after cardioplegic arrest with an oxygenated crystalloid solution. Guyton, R.A., Dorsey, L.M.A. *et al. Journal of Thoracic and Cardiovascular Surgery* 1985; **89:** 877.

Aldosterone and prolactin responsiveness after prolonged treatment of congestive heart failure with captopril. Jungmann, E., Storger, H. *et al. European Journal of Clinical Pharmacology* 1985; **28:** 1.

Usefulness and safety of cimetidine in patients receiving mexiletine for ventricular arrhythmia. Klein, A.L., Sami, M.H. *American Heart Journal* 1985; **109:** 1281.

Digoxin-trimethoprim interaction. Petersen, P., Kastrup, J. *et al. Acta Medica Scandinavica* 1985; **217:** 423.

Aggravation of ventricular arrhythmia. A drug-induced complication. Podrid, P.J. *Drugs* 1985; 29 Suppl 4: 33.

Regular review: therapeutic ranges in anti-coagulant administration. Poller, L. *British Medical Journal* 1985; **290:** 1683.

Comparative efficacy of transvenous cardioversion and pacing in patients with sustained ventricular tachycardia. Saksena, S. *et al. Circulation* 1985; **72:** 153.

New directions in cardiac imaging. Skorton, D.J., Collins, S.M. *Annals of Internal Medicine* 1985; **102:** 795.

The cardiovascular effects of regular and decaffeinated coffee. Smits, P., Thien, T., Van't Laar, A. *British Journal of Clinical Pharmacology* 1985; **19:** 852.

Effects of verapamil on calcium-induced rigidity and on filterability of red blood cells from healthy vols and patients with progressive systemic sclerosi. Sowemimi-Coker, S.O., Kovacs, I.B. *et al. British Journal of Clinical Pharmacology* 1985; **19:** 731.

Hospital readmissions among survivors six months after myocardial revascularization. Stanton, B.A., Jenkins, C.D. *et al. Journal of the American Medical Association* 1985; **253:** 3568.

Effect of digoxin on total body potassium. Swaminathan, R. *Clinical Physiology and Biochemistry* 1985; **3:** 204.

Deleterious effects of cardiopulmonary bypass—a prospective study of bubble versus membrane oxygenation. Vanoevern, W. Kazatchkine, M.D. *et al. Journal of Thoracic and Cardiovascular Surgery* 1985; **89:** 888.

Pharmacokinetics of verapamil in patients with renal failure. Vonbaak, M. *et al. European Journal of Clinical Pharmacology* 1985; **28:** 405.

The membrane and the lesions of storage in preserved red cells. Wolfe, L.C. *Transfusion* 1985; **25:** 185.

Acute hemodynamic and electrophysiologic effects of propranolol in patients receiving diltiazem. Wolfe, C.L. *et al. American Journal of Cardiology* 1985; **56:** 47.

Respiration

Physiology

The effect of low density gas breathing on vesicular lung sounds. Austrheim, O., Kraman, S.S. *Respiration Physiology* 1985; **60:** 145.

Role of daytime hypoxemia in the pathogenesis of right heart failure in the obstructive sleep apnea syndrome. Bradley, T.D. *et al. American Review of Respiratory Disease* 195; **131:** 835.

Ventilatory acclimatization to hypoxia is not dependent on arterial hypoxemia. Bush, M.A., Bisgard, G.E., Forster, H.V. *Journal of Applied Physiology* 1985; **58:** 1874.

Ventilatory control in normal man following five minutes' exposure to hypoxia. Davidson, A.C., Cameron, I.R. *Respiration Physiology* 1985; **60:** 227.

The alveolar macrophage. Du Bois, R.M. *Thorax* 1985; **40:** 321.

Work of breathing in patients with chronic obstructive pulmonary disease in acute respiratory failure. Fleury, B. *et al. American Review of Respiratory Disease* 1985; **131:** 822.

Respiratory mechanical effects of abdominal distension. Gilroy, R.J., Lavietes, M.H. *et al. Journal* *of Applied Physiology* 1985; **58:** 1997.

Respiratory muscle fatigue: a cause of ventilatory failure in septic shock. Hussain, S.N.A., Simkus, G., Roussos, C. *Journal of Applied Physiology* 1985; **58:** 2033.

Effects of the rebreathing pattern on pulmonary tissue volume and capillary blood flow. Kallay, M.C., Hyde, R.W. *et al. Journal of Applied Physiology* 1985; **58:** 1881.

Peripheral chemoreceptors in respiratory oscillations. Lahiri, S., Hsiao, C. *et al. Journal of Applied Physiology* 1985; **58:** 1901.

Studies of sympatho-adrenal reactivity and adrenoceptor function in bronchial asthma. Larsson, K. *European Journal of Respiratory Diseases* 1985; **66:** 1.

Pulmonary hypertension. Michael, J.R., Summer, W.R. *Lung* 1985; **163:** 65.

Dynamics of respiratory drive and pressure during NREM sleep in patients with occlusive apneas. Onal, E., Leech, J.A., Lopata, M. *Journal of Applied Physiology* 1985; **58:** 1971.

Altered breathing pattern elicited by stimulation of abdominal visceral afferents. Prabhakar, N.R., Marek, W., Loeschcke, H.H. *Journal of Applied Physiology* 1985; **58:** 1755.

Respiratory mechanics in mechanically ventilated patients with respiratory failure. Rossi, A., Gottfried, S.B. *et al. Journal of Applied Physiology* 1985; **58:** 1849.

Effect of acute pulmonary hypertension on pressure/flow in the canine pulmonary vascular bed. Selkurt, E.E. *Respiration Physiology* 1985; **60:** 169.

Decay of inspiratory muscle pressure during expiration in conscious humans. Shee, C., Ploy-Song-Sang, Y., Milic-Emili, J. *Journal of Applied Physiology* 1985; **58:** 1859.

Postural hypoxemia in cystic fibrosis. Stokes, D.C., Wohl, M.E.B. *et al. Chest* 1985; **87:** 785.

Changes in ventilation and its components in normal subjects during sleep. Stradling, J.R., Chadwick, G.A., Frew, A.J. *Thorax* 1985; **40:** 364.

Treatment and medication

Mechanical and ventilatory support. Cane, R.D., Shapiro, B.A. *Journal of the American Medical Association* 1985; **254:** 87.

Mechanical ventilation for acute postoperative respiratory failure after surgery for bronchial carcinoma. Hirschler-Schulte, C.J.W. *et al. Thorax* 1985; **40:** 387.

Modification of pulmonary oxygen toxicity by bleomycin treatment. Matalon, S., Harper, W.V. *et al. Journal of Applied Physiology* 1985; **58:** 1802.

Aerosol deposition in man. Newman, S.P., Pavia, D. *Aerosols in Medicine—Principles, Diagnosis and Therapy* 1985; 193.

Chlorpromazine—a specific effect on breathlessness? O'Neill, P.A., Morton, P.B., Stark, R.D. *British Journal of Clinical Pharmacology* 1985; **19:** 793.

Bioavailability and diuretic effect of furosemide during long-term treatment of chronic respiratory failure. Ogata, H., Kawatsu, Y. *et al. European Journal of Clinical Pharmacology* 1985; **28:** 53.

Pharmacokinetics of inhaled drugs. Pauwels, R. In: *Aerosols in Medicine-Principles* 1985; Ed. F. Moren, M.T. Newhouse, M.B. Dolovich: 219.

Helium–oxygen breathing in severe chronic obstructive pulmonary disease. Swidwa, D.M., Montenegro, H.D. *et al. Chest* 1985; **87:** 790.

Central nervous system

Physiology

Obstructive sleep apnea syndrome caused by oral cyst: a case report. Alving, J., Hojer-Pedersen, E. *Acta Neurologica Scandinavica* 1985; **71:** 408.

Cerebral blood flow and CO_2 responsiveness as an indicator of collateral reserve capacity in patients with carotid arterial disease. Bullock, R., Mendelow, A.D. *et al. British Journal of Surgery* 1985; **72:** 348.

Sympathetic outflow in man after anaesthesia of the glossopharyngeal and vagus nerves. Fagius, J., Wallin, B.G. *et al. Brain* 1985; **108:** 423.

Severe obstructive sleep apnea. I. onset, clinical course, and characteristics. Kales, A., Cadieux, R.J. *et al. Journal of Chronic Diseases* 1985; **38:** 419.

Severe obstructive sleep apnea. II. associated psychopathology and psychosocial consequences. Kales, A., Caldwell, A.B. *et al. Journal of Chronic Diseases* 1985; **38:** 427.

Impact of 70% nitrous oxide administration on regional distribution of brain blood flow in unmedicated healthy swine. Manohar, M. *Journal of Cardiovascular Pharmacology* 1985; **7:** 463.

Treatment and medication

Current application of high-dose steroid therapy for CNS injury—a pharmacological perspective. Braughler, J.M., Hall, E.D. *Journal of Neurosurgery* 1985; **62:** 806.

Indomethacin-mediated improvement following middle cerebral artery occlusion in cats—effects of anesthesia. Dempsey, R.J., Roy, M.W. *et al. Journal of Neurosurgery* 1985; **62:** 874.

Long-term use of dopamine agonists in Parkinson's disease. Jankovic, J. *Clinical Neuropharmacology* 1985; **8:** 131.

Distribution of sodium valproate in normal whole blood and in blood from patients with renal or hepatic disease. Jellett, L.B. *et al. European Journal of Clinical Pharmacology* 1985; **28:** 447.

Assessment of cardiac and respiratory function during surgery on patients with acute quadriplegia. Mac-

Kenzie, C.F., Shin, B. *et al. Journal of Neurosurgery* 1985; **62:** 843.

Cerebrospinal fluid uptake and peripheral distribution of centrally acting drugs: relation to lipid solubility. Ochs, H.R., Greenblatt, D.J. *et al. Journal of Pharmacy and Pharmacology* 1985; **37:** 428.

The pharmacology of myoclonus. Pranzatelli, M.R., Snodgrass, S.R. *Clinical Neuropharmacology* 1985; **8:** 99.

Successful treatment of neuroleptic-induced akathisia with baclofen and clonazepam. A case report. Sandyk, R. *European Neurology* 1985; **24:** 286.

Endocrine and metabolic

Physiology

Measurement of blood cortisol and acid output in patients with duodenal ulceration and normal subjects during insulin hypoglycaemia. Athow, A.C., Sewerniak, A.T. *et al. Clinical Science* 1985; **69:** 37.

Cushing's disease. Burch, W.M. *Archives of Internal Medicine* 1985; **145:** 1106.

Thyroid hormones and brain development: modulation of the binding activity of the T3 nuclear receptor by chromatin-associated factors. De Nayer, P., Dozin, B. *Molecular Physiology* 1985; **7:** 303.

Plasma norepinephrine, epinephrine, and dopamine levels in end-stage renal disease. Elias, A.N., Vaziri, N.D., Maksy, M. *Archives of Internal Medicine* 1985; **145:** 1013.

The relationship of plasma catecholamines to acute metabolic and hormonal responses to injury in man. Frayn, K.N., Little, R.A. *et al. Circulatory Shock* 1985; **16:** 229.

Signals from the oropharynx may contribute to the diuresis which occurs in man to drinking isotonic fluids. Gebruers, E.M., Hall, E.J. *et al. Journal of Physiology* 1985; **363:** 21.

Pharmacokinetic and clinical aspects of intensified subcutaneous insulin therapy. Lauritzen, T. *Danish Medical Bulletin* 1985; **32:** 104.

Whole-body protein breakdown and 3-methylhistidine excretion during brief fasting, starvation and intravenous repletion in man. Lowry, S.F. *et al. Annals of Surgery* 1985; **202:** 21.

Hypoglycemia: causes, neurological manifestations, and outcome. Malouf, R., Brust, J.C.M. *Annals of Neurology* 1985; **17:** 421.

Lactate dehydrogenase isoenzymes in diabetic patients. Nair, R.M.G., Menon, M.P. *et al. Clinical Physiology and Biochemistry* 1985; **3:** 157.

How insulin resistant are patients with noninsulin-dependent diabetes mellitus? Reaven, G.M., Chen, Y.D.I. *et al. Journal of Clinical Endocrinology and Metabolism* 1985; **61:** 32.

Effect of intravenous ketanserin on plasma catecholamines and renin activity in normal volunteers. Reimann, I.W., Ratge, D. *et al. European Journal of Clinical Pharmacology* 1985; **28:** 273.

Size of acute myocardial infarcts in patients with diabetes mellitus. Rennert, G., Saltz-Rennert, H. *et al. American Journal of Cardiology* 1985; **55:** 1629.

Release of gastrointestinal hormones in cardiodepressive shock. Revhaug, A., Lygren, I. *et al. Acta Anaesthesiologica Scandinavica* 1985; **39:** 371.

Pituitary-adrenal responsiveness to corticotropin-releasing hormone in patients receiving chronic, alternate day glucocorticoid therapy. Schurmeyer, T.H., Tsokos, G.C. *et al. Journal of Clinical Endocrinology and Metabolism* 1985; **61:** 22.

Complement activation and clearance in acute illness/injury—evidence for C5a as a cell-directed mediator of adult respiratory distress syndrome in man. Solomkin, J.S., Cotta, L.A. *et al. Surgery* 1985; **97:** 668.

Deranged alpha-adrenergic regulation of growth hormone secretion in poorly controlled diabetes—reversal of the exaggerated response to clonidine. Topper, E., Gertner, J. *et al. Pediatric Research* 1985; **19:** 534.

Diabetic gastroparesis: an abnormality of gastric emptying solids. Wright, R.A., Clemente, R., Wathen, R. *American Journal of the Medical Sciences* 1985; **289:** 240.

Corticotropin-releasing factor stimulation of adrenocorticotropin and beta-endorphin release: effects of acute and chronic stress. Young, E.A., Akil, H. *Endocrinology* 1985; **117:** 23.

Lack of effect of im diazepam administration on hGH and hPRL secretion in normal and acromegalic subjects. Zaccaria, M., Giordano, G. *et al. Journal of Endocrinological Investigation* 1985; **8:** 167.

Endocrine and metabolic

Treatment and medication

Ca antagonists do not alter aldosterone secretion during established Na depletion. Johnson, E.I.M., McDougall, J.G. *et al. American Journal of Physiology* 1985; **248:** E676.

Pharmacokinetics and pharmacodynamic effects of furosemide in patients with liver cirrhosis. Traeger, A. *et al. International Journal of Clinical Pharmacology, Therapy and Toxicology* 1985; **23:** 129.

Pain

Physiology

Substance P and the sensory innervation of intracranial and extracranial feline cephalic arteries: implications for vascular pain mechanisms in man. Norregaard, T.V., Moskowitz, M.A. *Brain* 1985; **108:** 517.

Treatment and medication

Epidural electrical stimulation in severe limb ischemia: pain relief, increased blood flow, and a possible limb-saving effect. Augustinsson, L.E. *et al. Annals of Surgery* 1985; **202:** 104.

Pain measurement: an overview. Chapman, C.R., Casey, K.L. *et al. Pain* 1985; **22:** 1.

The treatment of cancer pain. Foley, K.M. *The New England Journal of Medicine* 1985; **313:** 84.

Treatment of backache with spinal injections of local anesthetics, spinal and systemic steroids. A review. Kepes, E.R., Duncalf, D. *Pain* 1985; **22:** 33.

Anaesthesia, 1986, Volume 41, pages 106–119

News and notices

Stop Press. *Readers of this section are also referred to the Stop Press page at the end of this section.*

Obituaries

Ahuja, Bikram, MD, FFARCS. Senior registrar in anaesthetics, University Hospital of Wales, Cardiff. Qualified in Poona, India in 1972.

Bomonji, Terence Rupert, MRCS, LRCP, FFARCS, DA. Consultant anaesthetist to Dudley Area Health Authority. Qualified at St Bartholomew's Hospital in 1941.

Boyd, John, MD, FFARCS. Late anaesthetist to Royal Belfast Hospital for Sick Children and Royal Victoria Hospital, Belfast. Qualified at University of Belfast in 1926.

Brown, Alexander, MB, ChB, FFARCS, DA. Formerly consultant anaesthetist to the Hull and East Riding hospitals. Qualified at Aberdeen University in 1936.

Dunkin, Larence Joseph Francis Xavier, MB, BCh, BAO, FFARCS. Consultant anaesthetist to Newcastle General Hospital. Qualified at St Vincent's Hospital, Dublin in 1949.

France, John Malcolm, FFARCS. Late consultant anaesthetist to Northallerton General Hospital. Qualified at the University of Leeds in 1959.

Hawksley, Margaret, LVO, MB, BS, FFARCS. Formerly consultant anaesthetist to the Hospital for Sick Children, Great Ormond Street, London. Qualified at University College Hospital, London in 1930.

Hoggins, Eileen Mary, MB, ChB, FFARCS, DA. Formerly senior consultant anaesthetist to the Walsall hospitals. Qualified at Birmingham Medical School in 1943.

Jones, William Alyn, MRCS, LRCP, DA. Formerly anaesthetist to Hertford Co. Hospital and Queen Elizabeth II Hospital and Welwyn Garden City Hospital. Qualified St Mary's Hospital in 1936.

Odell, John Robert, MB, BS, FFARCS. Formerly consultant anaesthetist at The Royal Free Hospital. Qualified at the Middlesex Hospital in 1937.

Pinson, Kenneth Bernard, MB, ChB, FFARCS. Late consultant anaesthetist to Manchester Royal Infirmary. Senior member of the Association of Anaesthetists of Great Britain and Ireland. Qualified from Birmingham, 1914.

Rose, Thea Gwyneth Tesorina, MB, BS, DCH, DA. Latterly head of the anaesthetic department of Mpilo Hospital, Bulawayo, Zimbabwe. Qualified at University College Hospital and the West London Hospital Medical College in 1950.

Youngman, Harold Rowell, MD, FFARCS. Formerly honorary anaesthetist to United Cambridge Hospitals. Qualified at University of Cambridge and St Thomas's Hospital in 1926.

Association of Anaesthetists of Great Britain and Ireland

The Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA, England. Telephone: 01–631 1650 (Ansafone service available out of office hours).

Officers 1985–86

President: Dr T.B. Boulton (*Reading and Oxford*).
Immediate Past President: Professor M.D. Vickers (*Cardiff*).
President-Elect: Professor M. Rosen (*Cardiff*).
Vice-President: Professor J.P. Payne (*London*).
Vice-President: Dr Jean Horton (*Hong Kong*).
Vice-President: Dr W.R. MacRae (*Edinburgh*).
Honorary Treasurer: Dr M.M. Burrows (*Wirral*).
Honorary Secretary: Dr M.T. Inman (*Plymouth*).
Assistant Hon. Secretary: Dr P. Morris (*Manchester*).
Editor: Dr J.N. Lunn (*Cardiff*).
Assistant Editors: Dr M. Morgan (*Royal Postgraduate Medical School, London*), Dr C.E. Blogg (*Oxford*), Dr R. Greenbaum (*University College Hospital, London*), Dr R.M. Jones (*Guy's Hospital, London*).

Council 1985–86

All Officers with the exception of the Assistant Editors are *ex-officio* members of Council.

Elected Members: Professor A.P. Adams (*Guy's Hospital, London*), Dr W.L. Baird (*Glasgow*), Dr Elizabeth Bradshaw (*Ealing*), Dr K. Budd (*Bradford*), Dr R.J. Eltringham (*Gloucester*), Dr W.H.K. Haslett (*Belfast*), Dr D.J. Hatch (*Great Ormond Street, London*), Professor W.S. Nimmo (*Sheffield*), Dr T.W. Ogg (*Cambridge*), Dr J.F. Searle (*Exeter*), Professor G. Smith (*Leicester*), Dr W.S. Wren (*Dublin*), Dr Wendy Scott (*Chairman, Junior Anaesthetists' Group*), Dr G.W. Hamlin (*Secretary JAG*).

Annual Scientific Meeting, Leicester, 11–13 September 1985

The Scientific programme was as follows.

Symposium: Postoperative pain; Chairman: Dr K.A. Stewart. Measurement of pain, Professor G. Smith (*Leicester*). Pharmacokinetics of analgesic drugs, Professor W.S. Nimmo (*Sheffield*). *Guest Lecture*; Postoperative respiratory function and analgesia, Professor P.R. Bromage (*Denver, USA*).

Symposium: Computers and anaesthesia; Chairman: Dr A.R. Aitkenhead (*Leicester*). Anaesthetic records, Dr G.N.C. Kenny (*Glasgow*). Anaesthetic rotas, Dr J.N. Horton (*Cardiff*). EEG and evoked potentials, Dr P.S. Sebel (*London*). Closing the loop, Professor W.W. Mapleson (*Cardiff*).

Free Papers: Chairman: Dr D. Fell (*Leicester*). Age and speed of injection affect toxicity of propofol, Dr F.P. Robinson (*Belfast*). Anaesthesia for paediatric adenotonsillectomy, Dr P.J. Stow (*Northampton*). Anaesthesia for Nd-YAG laser surgery, Dr K.C. Moore (*Oldham*). Infiltration of the mesosalpinx with bupivacaine 0.5% effectively relieves pain following laparoscopic tubal sterilisation, Dr B.V. Wetchler (*Illinois, USA*). Active carbon dioxide absorption in anaesthesia, Dr J.V.I. Young (London). Report on a visit to the USA, Dr C.D. Hanning (*Leicester*).

Symposium: Modern trends in anaesthesia; Chairman: Dr C.D. Hanning. The anaesthetist and laser surgery, Dr A.C. Wainwright (*Southampton*). The anaesthetist and microsurgical techniques, Dr A. Loach (*Oxford*). Hypotensive anaesthesia, Dr J.A.W. Wildsmith (*Edinburgh*). Anaesthesia and psychiatric disease, Dr R.M. Jones (*Guy's Hospital, London*).

Symposium: Chronic pain; Chairman: Professor G. Smith. Pain clinic organisation, management and training, Dr K. Budd (*Bradford*). Drug therapy, Professor J.W. Thompson (*Newcastle upon Tyne*). The needle effect, Dr A.J.R. Macdonald (*Charing Cross*). Psychiatric management of chronic pain—an inpatient programme, Professor M.R. Bond (*Glasgow*). Special lecture with demonstration; Hypnosis, Dr B.D.L. Johnson, Emeritus Consultant Anaesthetist (*Leicester*).

The *John Snow Memorial Lecture* was given by Dr E.D. Acheson, Chief Medical Officer (*Department of Health and Social Security*).

Poster presentations: Dose reponse relations of Nalmefene and fentanyl, Dr T.C. Smith (*Chicago, Illinois*). Nerve blocks with butyl-amino-benzoate suspension for the control of chronic pain syndromes, Dr M. Shulman (*Chicago, Illinois*). The Datex relaxograph: A comparison with a force transducer, Dr J.A. Carter (*London*). An assessment of oral and intramuscular ranitidine and sodium citrate in obstetric anaesthesia, Dr R. Colman (*London*). Complete reversal of deep pancuronium block requires at least 20 minutes, Dr D.R. Goldhill (*Boston, Mass.*). Effect in dogs of beta blockade on potassium release after succinylcholine, Dr D.R. Goldhill (*Boston, Mass.*). The clinical pharmacology of high dose atracurium, Dr R.P.F. Scott (*Boston*). Gascard, an anaesthesia records program, Dr J.R. Davies (*Lancaster*). A computerised study of muscle relaxation during laparoscopy, Dr S.C. Allen (*Reading*). Hormonal response during ketamine anaesthesia, Dr M.H.W. Abdulla (*Basrah, Iraq*). Incidence of serological markers for Hep B infection amongst anaesthetists, Dr M.W. Ashby (*Oxford*). Halothane attenuates cardiopulmonary baroreflexes, Dr T.J. Ebert (*Milwaukee, Wis.*). Herpes zoster ophthalmicus pain responds to stellate ganglion block therapy, Dr B.V. Wetchler (Illinois). Does aminophylline antagonise midazolam? Dr W. Holmes (*Ballymena*). A new neonatal respiratory monitor, Dr C.D. Hanning (*Leicester*).

There were 480 registrants at this Meeting, which took place at the Leicester Polytechnic. The social programme started on the Wednesday evening with a buffet supper, generously contributed by the Leicestershire Area Health Authority, with entertainment by the 'Abracadabrets'. The accompanying persons' programme included a coach trip to Burghley House, followed by lunch at Stamford and then into the countryside of Rutland. The Lord Mayor of Leicester was host at a Civic Reception and Buffet at The De Montfort Hall, Leicester, with music provided by the orchestra of the Judge Meadows Community College. The Annual Dinner was held in the Grand Hotel, Leicester and was preceded by a reception, courtesy of the Sheffield and East Midlands Anaesthetic Society. The toast to the Association was given by Professor R. Dyson (*University of Keele*) and to whom the President, Dr T.B. Boulton replied and proposed the health of the guests. The Very Reverend Lawrence Jackson, Provost of Blackburn replied on behalf of the guests.

There were more than seventy firms who exhibited during the meeting and once again it was a pleasure to thank them for their enthusiastic participation.

The Annual General Meeting was attended by 140 members. The John Snow Silver Medal was awarded to Professor T.J. Gilmartin, who was unfortunately unable to be present.

Honorary Membership was conferred upon Dr G. Jackson Rees (*Liverpool*). Pask Certificates of Merit were presented to Dr W.M. Brown (*Belfast*), Dr

Margaret L. Heath (*London*), Cyril Jones Esq. (*East Grinstead*). These elections and awards were greeted with acclaim. Pask Certificates were also presented to Professor Dr med Dietrich F. Kettler, President of the German Society of Anaesthetists and Professor Dr med Hörst O. Stoeckel, at the Joint Meeting with the German Society of Anaesthetists in Bonn, in May 1985.

This Annual Scientific Meeting was a great success and all credit must go to the Organising Committee in Leicester for their hard work. The Organising Committee was Dr A.R. Aitkenhead, Professor G. Smith, Dr H. James, Dr D.G. Lewis, Dr M. Hampson, Dr D. Raitt, Mrs E. Smith, Mrs M. Turner, Dr K.A. Stewart, Dr A. Vickers, Dr A. May, Dr Margaret Chambers, Dr Fiona Thompson, Dr D. Fell and Dr I. McLellan (Chairman). The Association is very grateful to them all.

Future Meetings of the Association

Annual Scientific Meetings

1986—London, 18–19 September.
1987—Sheffield, 10–11 September.
1988—Southampton, 15–16 September.

Linkman Conferences

1986—London, 17 September.
1987—Sheffield, 9 September.
1988—Southampton, 14 September.

Membership subscriptions

Direct debit

Members resident in the United Kingdon are reminded of the advantages of the Direct Debit method of payment. Annual subscriptions can only be raised by resolution at the Annual General Meeting and members must be informed of any increase. Direct Debit forms can be obtained from the Honorary Treasurer. Overseas members, unless they have a United Kingdom bank account, should pay by cheque or Banker's draft. Members not wishing to use the Direct Debit system should pay by cheque.

Research grants

Research grants may be made towards a salary for a doctor or technician, or the cost of equipment. Candidates should write for full information to the Honorary Secretary and applications should be made on the special form designed for this purpose. Grants are unlikely to exceed £5000 per annum to an individual or department. Applications may be submitted any time during the year for consideration at the next meeting of the Research and Education Committee. This Committee meets three times each year.

Association travel grants

Association travel grants are available towards the cost of a tour, either at home or abroad, including teaching research or study, but neither for the purposes of attending meetings of societies nor for taking up posts abroad. Grants of up to £500 may be awarded.

Applications should be made on a special form which may be obtained from the Honorary Secretary and may be submitted at any time during the year, provided sufficient time is allowed for their consideration by the Research and Education Committee.

Awards for educational visits to third world countries

Council has recently created an additional award for those who are making relatively prolonged visits, normally of not less than one year, to countries to assist with the teaching of anaesthesia. These awards would offer sums of up to £1000 towards expenses incurred.

Applications should be made to the Honorary Secretary and may be submitted at any time of the year.

Association Travenol Travelling Fellowship

Travenol Laboratories have endowed a travelling fellowship to the value of £2500, while will be awarded on an annual basis and is open to all members of the Association of Anaesthetists. The award may be used for travel within the United Kingdom or overseas to undertake a hospital-based study to examine current problems, new ideas, fresh applications or alternative systems in the following fields: intravenous fluid therapy, parenteral nutrition, intravenous administration of drugs, blood and blood component therapy, intravenous solution and transfusion fluid filtration, or education and training in regard to any of these.

Applications for the 1986 award, which should enclose a summary of at least 1000 words giving details of the objectives of the proposed study, should be sent to the Honorary Secretary from whom further information may be obtained, before 1 February 1986.

Fees for Anaesthetists in independent practice in the United Kingdom

Guidelines on the scale of fees which should be charged in independent practice have been prepared by the Association and revised January 1986. Copies of this information can be obtained from the Honorary Secretary.

Central catalogue of historical books and equipment

A central national catalogue of the location of historical anaesthetic equipment and books is being prepared by the Association Archivist, Dr T.B. Boulton (*Oxford and Reading*). Dr D. Wilkinson (*St Bartholomew's Hospital*) is preparing a catalogue of apparatus and Dr I. MacLellan (*Leicester*) is preparing the catalogue of books. The Honorary Secretary would be grateful to receive lists of historical equipment and books from members who have them in their charge.

Publications of the Association of Anaesthetists of Great Britain and Ireland

Your anaesthetic, an explanatory leaflet for patients, 1978. *Anaesthetic record cards*, suitable for independent medical practice, 1978. *The role of the anaesthetist*, an exploratory study by Miss Lisl Klein, 1980. *Report of a Working Party on the use of controlled drugs in operating theatres*, 1982. *Report of a Working Party on assistance for anaesthetists*, 1983. *Staffing in a District General Hospital*, 1983. *Workload for consultant anaesthetists*, (revised) 1984. *Fees in independent practice*, 1984. *Workload for consultant anaesthetists*, implications of reductions in junior staff and the consultant only hospital, 1984. *Anaesthetic service in isolated units in the United Kingdom* (prepared jointly with the Anaesthetists' Sub-committee of CCHMS), 1984. *Consultant Advisory Appointments Committees*, results of a questionnaire, 1984. *Scavenging in theatres*, results of a questionnaire 1984. *Anaesthesia, A Career Guide*, an illustrated booklet designed to inform senior medical students and preregistration house officers of the value of postgraduate training in anaesthesia (recently revised to include information on the new examination system) 1984. *Professional References in the National Health Service*, guidance and proforma, 1985. *Post-Anaesthetic Recovery Facilities*, 1985.

'Near Miss' reporting

Council of the Association intends to publish, from time to time, instructive examples of 'near-misses' which have educational value whether or not they led to any serious morbidity or mortality. Readers are invited to submit accounts of the genesis, detection and correction of incidents, giving sufficient detail as to make the matter intelligible to practising anaesthetists and to point out the educational aspect.

Reports should generally be between 150–500 words in length but submissions may be longer than this and will be edited if necessary. They will be published anonymously.

Editorial work will be undertaken after the secretariat has removed any trace of personal identification. The style aimed for will be on the lines of clinical incidents currently published by the defence societies. Please submit any incidents you think worthy of report to the Honorary Secretary, Critical Incident Reports, at the Association offices.

Undergraduate prize of the Association

The Prizes are offered for the most meritorious essays written by an undergraduate medical student at a university in Great Britain or Ireland. The competition is in two classes with prizes in each class of £100, £50 and £25.

Class 1—aspects of basic science of anaesthesia.
Class 2—clinical aspects of anaesthesia.

Rules

Essays should be submitted before 1 April 1986. The number of entrants from any one medical school is limited to a maximum of five. The Association recognises that most medical schools already offer prizes to medical students for an essay on a topic related to the specialty and has therefore decided that the winning of a local prize will not preclude the writer from entering for the Association prize.

Essays should be prepared according to the general format of the 'Notice to Contributors' at the end of each issue of *Anaesthesia*. Three copies of the essay should be forwarded to the Honorary Secretary.

Regional and Specialist Society Meeting Dates

The Honorary Secretary once again appeals to the secretaries of regional and specialist anaesthetic societies to try to check that their proposed meetings do not conflict with other previously arranged events to their mutual detriment. Dr A. Padfield, Royal Hallamshire Hospital, Sheffield S10 2RX, sub-editor of the National and local events section, has advance notice of meeting dates beyond those published in that section.

Competence to practise

The Association of Anaesthetists of Great Britain and Ireland and the Royal College of Psychiatrists are cooperating in a scheme to help sick anaesthetists early in their illness.

The system depends upon voluntary reporting by colleagues and is not coercive. It must be emphasised that this scheme is supplementary to existing controls. Fitness to practise may be impaired through illness and the sick doctor for various reasons may not take any steps to remedy the situation. The scheme provides machinery whereby confidential psychiatric help can be offered to the ailing doctor from a source outside his own Region.

The reporting clinician should contact the office of the Association of Anaesthetists to ascertain the name of a referee (Dr P.J. Helliwell, Dr D.C. Howat, Dr S.A. Mason) and need not identify himself to the office staff. The reporting clinician will be given the name, telephone number and availability of the referee. Preferably, a second clinician will also be required to confirm the report to the referee. The referee will then contact a psychiatrist from another Region nominated by the College of Psychiatrists from a prepared list: the psychiatrist will then get in touch with the potential patient.

No further information will be transmitted through the system unless the potential patient does not accept the offer of a visit to the nominated psychiatrist. In that case, the reporting physician(s) will be informed after a month that treatment has not been accepted.

Suitable arrangements have been made for confidential treatment of the doctor–patient in another Region and for the reimbursement of travel expenses.

Other relevant publications

WFSA Cardiopulmonary Cerebral Resuscitation Manual. Those members wishing to receive a copy should send a stamped addressed envelope measuring not less than 175 × 250 mm and bearing stamps to the value of £1 (United Kingdom) to Dr P.J.F Baskett, Secretary–Treasurer, Cardiopulmonary Resuscitation Committee WFSA, at the Association offices.

WFSA Manual on Obstetric Analgesia and Anaesthesia. Copies of this manual are available to members for £2 plus 75p postage. Please send a stamp and addressed envelope to the Honorary Secretary at the Association offices.

Mortality associated with anaesthesia. The report on the Association's study was published by the Nuffield Provincial Hospital Trust (3 Prince Albert Road, London NW1 7SP) from whom copies may be purchased. Members of the Association who wish to receive a copy should send £1 (to cover postage and administrative charges) to the Association office with their request.

Guidelines for the basic facilities and equipment required for the administration of anaesthetics in hospitals in the European Economic Community, published by the UEMS (Anaesthesia and Intensive Care Committee). Photocopies are available from the Association office.

Ties

Ties (*old design*) are available in twinzine/terylene in navy, maroon or green, at £4.25p each, post free.

A new design of tie, which depicts the coat of arms of the Association is now available. The material and colours are similar to the old, the price is £4.75p (including inland postage). Orders including your cheque, to the Honorary Secretary.

Catalogues and slides of the Charles King collection of historical apparatus

The Development of Anaesthetic Apparatus. A History based on the Charles King Collection: Price £27.50 (£19.50 to Members of the Association of Anaesthetists or subscribers to *Anaesthesia*). Post and packing £1.75.

Colour Slides of the Charles King Collection. 8 sets of 12 slides. List on request. Prices: One set £5 (p & p 59p). 8 sets £37.50 (p & p £1.75). 8 sets plus the book *Development of Anaesthetic Apparatus* £55 (p & p £2.35).

These items can be ordered from the Association offices.

Souvenirs of the Golden Jubilee of the foundation of the Association of Anaesthetists of Great Britain and Ireland

The following commemorative souvenirs can be obtained by writing to the Association office.

Wall plaque of the Arms of the Association of Great Britain and Ireland in full heraldic colours (18 × 15 cm)	£12.00
Wall plaque of the badge of the World Federation of Societies of Anaesthesiologists (WFSA)	£12.00
Lead crystal glass tankard (0.6 litre) engraved with the Arms of the Association and inscribed 'Golden Jubilee 1932–1982' (limited edition of 250, in a presentation box)	£17.00
Fine bone china plate by Wedgwood. Marked limited edition of 250. Diameter 23 cm. Association Coat of Arms. (Gold with red and blue lettering on a white background, in a presentation box)	£15.00

Audiovisual material for sale or hire

The following audiovisual material is the property of the Association and may be bought or hired.

16-mm films

'Lest we forget—1' Four brief films made in conjunction with the Section of Anaesthetics of the Royal Society of Medicine, which record a meeting held in December 1974 under the Presidency of the late Dr C.J. Massey Dawkins. (Blind Nasal Intubation, Sir I.W. Magill; Spinal Analgesia, Sir R.R. Macintosh; Cyclopropane, Dr M.D. Nosworthy; Vinyl ether, Dr W. McConnell).

These films may be hired at the nominal charge of £8.50 each + postage. Copies can be ordered for purchase and quotations are available on enquiry.

Audiocassettes

These are for sale only. All four talks, from each meeting are on one cassette and no slides were used (£3.00).

'Lest we forget—1' This is a sound recording of the previously described meeting.

'Lest we forget—2' This is a sound recording of a second meeting held under the Presidency of Dr C.F. Scurr in March 1979. The contributors were: Sir G.S.W. Organe (the introduction of muscle relaxants), Professor A.C. Forrester (hypothermia), Dr A.I.P. Brown ('flat on one's face) and Dr J.A. Lee (spinal analgesia).

The Junior Anaesthetists' Group of the Association of Anaesthetists of Great Britain and Ireland

All junior members of the Association are members of the Group. The Group committee has representation on various committees of the Association and Faculty.

Committee

Chairman: Dr Wendy E. Scott (*12 Warden Hill, Everton, Sandy, Bedfordshire, Tel. (0767) 82747.* Advisory Committee, Council of the Association, House, Furnishing, Research and Education Committees).

Secretary: Dr G.W. Hamlin (*1 Grange Park Close, Leeds, LS8 3BU. Tel. 0532 659114.* Council of the Association. JCHTA Manpower and Working Party of Faculty, Advisory Panel and Faculty Tutors).

Committee members: Dr Laurie Allan (*Pentland Grove House, Seafield by Roslin, Midlothian, Edinburgh EH25 9RQ. Tel. (031) 445 2313.* Hospital Junior Staff Committee, Council of Royal Society of Medicine, Editorial Board.). Dr L. Conroy (*3 Elm Vale Court, Wilton, Cork, Eire. Tel (021) 46440*). Dr A.D.J. Nicoll (*2 Hardwick Close, Ipswich IP4 5XB. Tel. (0473) 718432.* Faculty Education Committee, Safety Committee, Linkman Coordinator). Dr I. Woods (*Ingfield, Milking Stile Lane, Lancaster LA1 5QD. Tel. (0524) 32129.* International Relations Committee). Dr Nancy Redfern (*Westfield House, Acomb, Hexham, Northumberland. Tel. (0434) 607444.* Specialist Societies Committee). Dr Deborah Shiller (*4 Lisa Court, Downsland Road, Basingstoke, Hants. Tel. (0256) 477885*). Dr Anne Blyth (*7 Cleveden Gardens, Glasgow G12 0PU. Tel. (041) 34 9974*). HJSC Representative on JAG. Dr A. Mackie (*33 St Fagan's Rise, Cardiff CF5 3EZ. Tel. (0222) 553084.* Coopted for Cardiff meeting). Dr K.C. Lowry (*10 Sandhill Park, Lurgan, Co. Armagh BT66 7AX.* Coopted for Northern Ireland meeting).

Representative of Council: Dr T.B. Boulton (*Reading*).

Doctors with domestic commitments

There was a meeting on June 15, 1985 held in Reading concerned with doctors with domestic commitments (DDC). Eighty-four people attended and discussed different aspects of the DDC training scheme as it is now and as it may become in the future. This worthwhile occasion provided a useful forum for these doctors to express their anxieties and helped to dispel any feeling of isolation which they were experiencing during training.

Annual Meeting

1986—Cardiff, 8–10 April (Junior Linkman Meeting, April 8).

Faculty of Anaesthetists of the Royal College of Surgeons of England

The Faculty of Anaesthetists of the Royal College of Surgeons of England, 35–43 Lincoln's Inn Fields, London WC2A 3PN. Telephone: 01–405 3474.

Faculty news

Dudley Buxton Prize

The Dudley Buxton Prize for 1986 has been awarded to Professor J.P. Payne.

Faculty medals

Faculty medals have been awarded to Dr G.E. Hale Enderby and Dr Barbara M.Q. Weaver.

New examiners

The following have been elected as additional new examiners for the Part I FFARCS exam for academic year 1985/86. Dr A. Eleri Edwards, Dr Penelope B. Hewitt, Dr M.J. Lindop, Dr D.A. Saunders, Dr A.B.M. Telfer, Professor J.E. Utting.

Nuffield Prize

The Nuffield Prize has been awarded to Dr Melanie Hearn on the results of the Part II FFARCS examination held in May 1985.

Examination results

At the Part II Fellowship examinations held in October 1985 70 of the 203 candidates were successful.

Faculty of Anaesthetists of the Royal College of Surgeons in Ireland

The Faculty of Anaesthetists of the Royal College of Surgeons in Ireland, 123 St Stephen's Green, Dublin 2.
Telephone: Dublin 780200 (Ext 268).

Dean: Dr P.W. Keane.
Vice-Dean: Dr D.C. Moriarty.
Honorary Secretary: Dr D.F. Hogan.
Honorary Treasurer: Dr J.C. Cooper.

The John Snow Silver Medal was presented to Professor T.J. Gilmartin by Dr T.B. Boulton, President, Association of Anaesthetists of Great Britain and Ireland after the Scientific Meeting in September 1985. The citation was read by Dr W.S. Wren.

Annual Scientific Meeting, 1986.

This meeting will be held on May 16–17 1986. There will be three topics: Adverse drug reactions, Anaesthetic applications of computers, and Muscle relaxants.

The *Gilmartin Lecture* will be delivered by Professor Sir J. Gordon Robson, CBE, DSc, FRCS, FFARCS, FFARCSI (Hon) on May 16.

Fellowship Examinations

The first part of the new three-part examination will be held on 25 April (orals start 28 April); part two, 26 May (orals start 27 May); and part three, 18 April (orals start 21 April). Further information may be obtained from the Administrative Officer, Faculty of Anaesthetists.

Section of Anaesthetics of the Royal Society of Medicine

Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE. Telephone: 01–580 2070

President: Dr Aileen K. Adams.
Secretaries: Dr I.M. Verner (*Department of Anaesthetics, The Middlesex Hospital, Mortimer Street, London W1N 8AA*), Dr G.M.C. Patterson (*Oxford*).

Meetings of the Section are held on the first Friday in the month, beginning in November, and are held at 1 Wimpole Street, London W1M 8AE, at 5.30 p.m.

Fellows of the RSM are welcome to bring guests if they wish.

Programme

1986

10 January—*Calcium and calcium antagonists.* Dr F.R. Ellis, Dr R.M. Jones, Dr H. Swanton.
7 February—*Joint meeting with the Section of Comparative Medicine. The evaluation of pain responses.* Professor J. Norman, Dr Barbara Weaver, Dr P.A. Flecknell, Dr V. Molony.
7 March—*Joint meeting with the United Services Section. High altitude hypoxia: rapid and slow acquisition.* Group Captain J. Ernsting, Dr J.S. Milledge.
18 April—*Hepatotoxicity of halothane—an enigma of drug toxicity.* Professor M.J. Cousins (*Australia*).
9 May—*May & Baker R.S.M. Prizes Essays. Annual General Meeting. Annual Dinner.*
6 June—*All-day symposium: Anaesthesia and ENT surgery.*

Specialist Societies

British Association for Immediate Care (BASIC)

Chairman: K.C. Easton, OBE.
Secretary: Hamish McLeod (*The Hope, Moffat Dumfrieshire. Tel: Moffat 20314*).

Society of Anaesthetists of the British Forces in Germany

President: Professor J.P. Payne (London).
Secretary: Major S.T. Inglis, FFARCS, RAMC (BMH Rinteln, BFPO 20 Germany).

Association of Cardiothoracic Anaesthetists

Honorary Secretary: Dr R.D. Latimer (*Papworth Hospital, Papworth Everard, Cambridge CB3 8RE. Tel: 0480 830541*).

Future meetings

1986—Inaugural Meeting of the European Association of Cardiovascular Anaesthetists.
17–18 June, Cambridge.
Information: Dr R.D. Latimer.
2–5 September, Munich
Society of Cardiovascular Anaesthetists.
Information: Dr J.A. Richter (*Sophienstrasse 1, 8000 Munchen 2*).
12 December, London.
Information: Dr R. Feneck (*London Chest*) *Hospital, Bonner Road, London E2 9JX*).
1987—Spring Meeting—Cambridge.
Information: Dr I. Hardy (*Papworth Hospital, Papworth Everard, Cambridge CB3 8RE*).
Autumn Meeting—Liverpool.
Organiser: Dr J.C. Richardson (*Broadgreen Hospital, Thomas Drive, Liverpool L14 3IB*).

Association of Dental Anaesthetists

President: Dr T.M. Young (*Manchester*).
Secretary: Dr M.A. Skivington (*Department of Anaesthetics, Poole General Hospital, Poole, Dorset BH15 2JB*).

Future meetings

1986—11 January. St George's Hospital, London.
Information: Dr Jane Stanford (*Department of Anaesthetics, St George's Hospital, Blackshaw Road, London SW17*).
27–28 June. Manchester Royal Infirmary.
Information: Dr T.M. Young (*Department of Anaesthetics, Royal Infirmary, Manchester M13*).
1987—17 January. Queen Elizabeth Hospital, Postgraduate Medical Centre, Birmingham.
Information: Dr P.J. Tomlin.
11 July. Plymouth.
Information: Dr F.S. Keddie.
1988—Spring. Guernsey.
Information: Dr P.D.M. Costen.

Intensive Care Society

Chairman: Dr Sheila M. Willatts (*Bristol*).
Meetings Secretary: Dr C.J. Hinds (*St Bartholomew's Hospital*).
Secretary/Treasurer: Dr D. Ryan (*Intensive Therapy Unit, Freeman Hospital, Newcastle upon Tyne NE7 7BE*).

Future meetings

1986—11–12 April. Newcastle upon Tyne.
1 November. Hospital for Sick Children, London.
1987—9–11 April. Exeter University.

Autumn meeting

This was held at University College Hospital on 5 October 1985. The Scientific programme was as follows. Management of acute chest trauma, Mr P. Goldstraw (*Brompton Hospital, London*); Brain protection, Professor E. Frost (*New York*); Training in intensive care —an update, Dr S.M. Willatts (*Bristol*); Long term results of mechanical ventilation, Dr J.F. Searle (*Exeter*); Severity scoring, Dr W. Knaus.

There was a Trade exhibition and the Annual General Meeting was held at the end of the meeting.

The Intractable Pain Society of Great Britain and Ireland

Chairman: Dr H. Rafferty (*Dublin*).
Vice Chairman/Chairman Elect: Dr K. Budd (*Bradford*).
Honorary Secretary: Dr T.P. Nash (*Basingstoke District Hospital, Aldermaston Road, Basingstoke, Hampshire RG24 9NA*).

Prize Essay

An annual competition is held for the best essays related to pain relief. Submissions to the Honorary Secretary by 31 August 1986. Essay contents are judged in two groups, Doctors in training and Society members.

Future meetings

1986—26–28 June. Belfast.
Hosts: Drs W.B. Loan, R. Armstrong and J. Cooper.
1987—Liverpool.
Host: Dr J.C. Wells.
1988—Basingstoke.
Hosts: Drs T.P. Nash and J.E. Hurley.

Neuroanaesthetists' Travelling Club

Information: Dr S.B. Foulds, Salford Health Authority, Peel House, Albert Street, Eccles, Manchester M30 0NJ.

Obstetric Anaesthetists' Association

President: Dr D.D. Moir (*Glasgow*).
Honorary Secretary: Dr J. Thorburn (*Department of Anaesthesia, The Queen Mother's Hospital, Yorkhill, Glasgow G3 8SH*).
Treasurer: Dr A.P. Rubin (*London*).
Minute Secretary: Dr B.R. Wilkey (*Cambridge*).
All UK membership enquiries to Dr J. Thorburn, please.

Future meetings

1986—21 March. Dundee, Scotland.

Information: Dr M.K. Milne (*Dept of Anaesthesia, Ninewells Hospital, Dundee, Scotland*).
4 September. Coleraine, Northern Ireland.
Information: Dr J. Moore (*Dept of Anaesthesia, Royal Victoria Hospital, Belfast, Northern Ireland*).

Autumn meeting

This was held at St George's Hospital, London on 20 September 1985. The scientific programme was as follows.

Session 1. *Chairman*, Inger Findley, Dr Sheila Cohen (*Stanford, USA*), The anaesthetist and the patient in preterm labour.

Session 2, *In vitro* fertilisation. *Chairman*, Professor G.C. Chamberlain (*St George's*). Methods and technique, Mr Ian Craft (*The Cromwell Hospital*). of IVF, Dr A.W. Macara (*Bristol*).

Session 3. *Chairman*, Dr A.C. Thurlow (*St George's*). Neurological damage following vaginal delivery, Dr M. Swash (*The London Hospital*). Intracranial pathology complicating pregnancy, Dr C. Beeby. Sickle cell disease in pregnancy, Dr Parker-Williams (*St George's*).

Session 4. *Chairman*, Dr D.D.C. Howat (*St George's*). Fibreoptic approach to epidural space, Dr B. Liban (*St George's*). The anatomy of the ligamentum flavum, Dr P.A. Gaynor (*New East Surrey Hospital*). The reproductive and teratogenic effects of nitrous oxide, halothane, isoflurane and enflurane in Sprague-Dawley rats, Professor I. Mazze MD (*Stanford, USA*).

Association of Paediatric Anaesthetists

President: Dr G.W. Black (*Belfast*).
Honorary Secretary: Dr P. Morris (*Royal Manchester Children's Hospital, Pendlebury, Manchester M27 1HA*).

Future meetings

1986—21–22 March. Annual Meeting. Sheffield.
Information: the Honorary Secretary.
28 May–4 June. Joint meeting with the Swedish Society of Anaesthetists in Gothenburg and Stockholm.
Information: Dr W.R. Hain (*University Hospital, Queen's Medical Centre, Nottingham NG7 2YH*).
1987—20–21 March. Leeds.
Information: the Honorary Secretary.

Plastic Surgery and Burns Anaesthetists

President: Dr C.C.M. Howie (*Bangour*).
Honorary Secretary: Dr F.J.M. Walters (*Department of Anaesthetics, Frenchay Hospital, Bristol BS16 1LE*).

Enquiries about membership to the Honorary Secretary, please.

Future meeting

1986—Whiston, Merseyside.
Information Dr C.S. Ince (*Department of Anaesthetics, St Helen's Hospital, St Helen's, Merseyside WA9 3EA*).

The Russell Davies and Stuart Laird Prize

The Society wishes to announce that this prize, £200, has been generously donated by Abbott Ltd. The prize will be awarded for an essay connected with anaesthesia and plastic and burns surgery and is open to any career anaesthetist in the National Health Service. Applications are invited for the prize which is to be awarded in October 1986. Further details are obtainable from the Honorary Secretary.

Anaesthetic Research Society

Chairman: Professor A.A. Spence.
Honorary Secretary: Dr A.R. Aitkenhead (*University Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW*).

Future meetings (closing dates for papers)

1986—11–12 April (28 February). University of Leeds.
4–5 July (May 23). University of Newcastle.
15 November (3 October). St Bartholomew's Hospital, London.

Special notice

Abstracts are photoreduced and must be submitted on a preprinted form, which is available from the Hon. Secretary. All correspondence and abstracts should be sent to the Hon. Secretary.

Resuscitation Council (UK)

Chairman: Mr A. Marsden.
Secretary: Dr D.A. Zideman (*Department of Anaesthetics, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS*).

Advanced life support

Posters which illustrate the Council's recommendations for Advanced Life support are now available.

Home news and notices

Academic appointments

Dr A.J. Asbury, PhD, FFARCS has been appointed Senior Lecturer in Anaesthetics in the University of Glasgow, Western Infirmary, Glasgow, G11 6NT.

Dr M. Rosen, FFARCS, has been appointed to an Honorary Chair in Anaesthetics for 5 years in the University of Wales. This is the first occasion that a consultant in the National Health Service has received this honour.

Dr M.A. Stafford, MSc, FFARCS has been appointed Senior Lecturer in Anaesthetics to the University of Newcastle-upon-Tyne.

Consultant appointments

Dr J.A. Andrews, Sunderland Health District.
Dr P. Barry, Gwynedd HD.
Dr W.R. Casson, Stirling Royal Infirmary.
Dr P.H. Chambers, Milton Keynes General Hospital.
Dr G.M. Duthie, Dr Gray's Hospital, Elgin.
Dr P. Elliott, Royal Victoria Hospital, Belfast.
Dr J.A. Emery-Barker, Dunfermline and West Fife Hospital.
Dr T. Ireland, Royal Alexandra Infirmary, Paisley.
Dr R. E. Jones, Harold Wood and Brentwood Hospitals.
Dr T. Kirwan, Westminster and St Stephen's Hospitals, London.
Dr A. McDonald, Falkirk and District Royal Infirmary.
Dr J.F. McGeachie, Oldham HD.
Dr A. McHutchon, Queen Elizabeth Hospital, Gateshead.
Dr S. Madsen, Argyll and Clyde Health Board.
Dr P.J. Morris, Addenbrooke's Hospital, Cambridge.
Dr M. Navaratnarajah, Croydon HD.
Dr E. Shanahan, The Adelaide Hospital, Dublin.
Dr T. Sivalingam, Bolton HD.
Dr P. Smith, Trent AHA.
Dr M.P. Tattersall, Princess Margaret Hospital, Swindon.
Major M.C. Thompson, Musgrove Park Hospital, Belfast.
Dr A.A. Tomlinson, North Staffordshire HD.
Dr K. Tusiewicz, Bloomsbury HD.
Dr D. McD. Watson, Northern RHA.
Dr D.M. Watson, West Cumberland Health District.
Dr C.G. Weston, Solihull HD.
Dr R.G. Wilkins, University Hospital of South Manchester.

Spahealth Limited

This organisation (*16 Great College Street, London, SW1*) has been set up to extend and improve audio-visual aids, particularly video tapes, for public and professional educational purposes. The parent company, Spafax Television, have considerable experience in the field which they now intend to extend to educational films associated with medicine, health, sport and nutrition. Further information can be obtained from the company concerned.

National and local events

The diary is collated by Dr A. Padfield, Consultant Anaesthetist, Royal Hallamshire Hospital, Sheffield S10 2RX. Society secretaries are invited to submit their programmes to him.

January 1986

3 *FFA Part 3* London. Written papers.

7 *FFA Part 1/DA (UK)* London. Applications due.

7 *Edinburgh & East of Scotland Society of Anaesthetists.* Mr Roger Catto, Hospital Budget Management.
Information: Dr D.G. Littlewood, Department of Anaesthetics, Royal Infirmary, Edinburgh EH3 9YW.

8 *Yorkshire Society of Anaesthetists.* Professor D. Campbell, *In Memoriam, Professor D.G. McDowall.*
Information: Dr J.S. Gibson, Department of Anaesthetics, Leeds General Infirmary, Leeds LS1 3EX.

10 *Section of Anaesthetics, Royal Society of Medicine.* Calcium and Calcium Antagonists.
Information: Sections Office, RSM, 1 Wimpole Street, London W1M 8AE.

11 *Association of Dental Anaesthetists.* At St George's Hospital, London.
Host: Dr Jane Stanford, Department of Anaesthetics, St George's Hospital, Blackshaw Road, London SW17 0QT.

14 *Reading Anaesthetists.* Title to be announced.
Information: Dr A. Marshall Barr, Department of Anaesthetics, Royal Berkshire Hospital, Reading RG1 5AN.

15 *Northern Ireland Society of Anaesthetists.* Dr M. Rosen, *Postoperative pain relief—If not now, when?*
Information: Dr J.E. Hegarty, Department of Anaesthetics, 97 Lisburn Road, Belfast BT9 7BL.

15 *Sheffield Anaesthetists.* Mr D. Price, *Management of head injuries.*
Information: Dr N.R. Bennett, Department of Anaesthetics, Royal Hallamshire Hospital, Sheffield S10 2RX.

16 *Manchester Medical Society, Section of Anaesthetics.* Prof. W.S. Nimmo, *Variability in drug response in anaesthesia.*
Information: Dr E.E.M. Thompson, Manchester Medical Society, University of Manchester, Oxford Road, Manchester M13 9PL.

17 *Liverpool Society of Anaesthetists.* Prof. A.A. Spence, *On the level.*
Information: Dr Anne Florence, Department of Anaesthetics, Broadgreen Hospital, Liverpool L14 3LB.

24 *Glasgow & West of Scotland Society of Anaesthetists.* 40th Anniversary Dinner.
Information: Dr D.S. Arthur, Royal Hospital for Sick Children, Glasgow G3 8SJ.

30 *Midland Society of Anaesthetists.* Registrar's Prize Meeting, George Eliot Hospital, Nuneaton.
Information: Dr S.M. Mostafa, Department of Anaesthetics, Selly Oak Hospital, Birmingham B29 6JD.

February 1986

3 *FFA Part 3* London, vivas begin.

4 *Edinburgh & East of Scotland Society of Anaesthetists.* Dr J. Wilson, *Presidential Address.*
Information: Dr D.G. Littlewood, Department of Anaesthetics, Royal Infirmary, Edinburgh EH3 9YW.

5 *Sheffield Anaesthetists.* Dr R. McNicholl, *Useful blocks in paediatric anaesthesia.*
Information: Dr N.R. Bennett, Department of Anaesthetics, Royal Hallamshire Hospital, Sheffield S10 2RX.

7 *Royal Society of Medicine, Section of Anaesthetics* (jointly with Comparative Medicine). The evaluation of pain responses.
Information: Sections Office, RSM, 1 Wimpole Street, London W1M 8AE.

11 *Reading Anaesthetists.* Title to be announced.
Information: Dr A. Marshall Barr, Royal Berkshire Hospital, Reading, Berks RG1 5AN.

12 *Yorkshire Society* AGM. Dr M.M. Burrows, *Current Medicopolitics.*
Information: Dr J.S. Gibson, Department of Anaesthetics, Leeds General Infirmary, Leeds LS1 3EX.

12 *Northern Ireland Society.* Presidential Address.
Information: Dr J.E. Hegarty, Department of Anaesthetics, 97 Lisburn Road, Belfast BT9 7BL.

15 *South East Thames Society.* At Guy's Hospital, London.
Information: Dr P.B. Hewitt, Department of Anaesthetics, Guy's Hospital, London SE1 9RT.

18 *FFA Part 1/DA (UK)* Papers London.

20 *Manchester Medical Society, Section of Anaesthetics* AGM. Papers for ICI & Abbott Registrars' Prizes.
Information: Dr E.E.M. Thompson, University of Manchester, Oxford Road, Manchester M13 9PL.

20 *North East of Scotland Society.* Registar's Papers.
Information: Dr G. Adey, Department of Anaesthetics, Aberdeen Royal Infirmary, Aberdeen.

21 *Liverpool Society.* Registrar's Prize Papers.
Information: Dr Anne Florence, Department of Anaesthetics, Broadgreen Hospital, Liverpool L14 3LB.

26 *Glasgow & West of Scotland Society.* Members' Night.
Hosts: Division of Anaesthesia, Royal Alexandra Infirmary, Paisley.
Information: Dr D.S. Arthur, Royal Hospital for Sick Children, Glasgow G3 8SJ.

March 1986

4 *Edinburgh & East of Scotland Society.* Members' Night.
Information: Dr D.G. Littlewood, Department of Anaesthetics, Royal Infirmary, Edinburgh EH3 9YW.

5 *FFARCS Part 2 applications due*, London.

5 *Northern Ireland Society.* Registrar's Prize.
Information: Dr J.E. Hegarty, Department of Anaesthesia, 97 Lisburn Road, Belfast BT9 7BL.

7 *Section of Anaesthetics, Royal Society of Medicine* (jointly with United Services). *High altitude hypoxia: rapid and slow acquisition.*
Information: Sections Office, RSM, 1 Wimpole Street, London W1M 8AE.

11 *Reading Anaesthetists.* Title to be announced.
Information: Dr A. Marshall Barr, Department of Anaesthetics, Royal Berkshire Hospital, Reading RG1 5AN.

13 *Sheffield & East Midlands Society* at Sheffield. *Paediatric Anaesthesia.*
Information: Dr D.F. Baigent, Leicester Royal Infirmary, Leicester LE1 5WW.

14–15 *Association of Paediatric Anaesthetists* at Sheffield.
Information: Dr P. Morris, Royal Manchester Children's Hospital, Manchester M27 1HA.

14 *Northern Ireland Society*. Conference & Annual Dinner.
Information: Dr J.E. Hegarty, Department of Anaesthetics, 97, Lisburn Road, Belfast BT9 7BL.

15 *Midland Society & Society of Anaesthetists of Wales* at Worcester.
Information: Dr S.M. Mostafa, Department of Anaesthetics, Selly Oak Hospital, Birmingham B29 6JD.

17 *FFA Part/DA (UK) vivas begin*, London.

19 *Faculty Anniversary Forum*. Ethics and medico legal matters. *Joseph Clover Lecture*.
Information: Secretary, Faculty of Anaesthetists, 35/43 Lincoln's Inn Fields, London WC2A 3PN.

20 *Current Trends in Chronic Pain Relief* at St Bartholomew's Hospital.
Information: Dr J.M.G. Foster, Department of Anaesthetics, St Bartholomew's Hospital, London EC1A 7BE.

20 *Manchester Medical Society, Section of Anaesthetics*; joint meeting with *Liverpool Society*. Dr B. Pollard, *Mixing relaxants*. Dr I. Campbell, *Metabolic aspects of feeding*.
Information: Dr E.E.M. Thompson, University of Manchester, Oxford Road, Manchester, M13 9PL.

21 *North of England Society of Anaesthetists*. Dr Felicity Reynolds, *Placental drug transfer*.
Information: Dr J.E. Charlton, Department of Anaesthetics, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP.

22 *Yorkshire Society*. All day meeting at Pontefract Hospital.
Information: Dr J.S. Gibson, Department of Anaesthetics, Leeds General Infirmary, Leeds LS1 3EX.

22 *Edinburgh & East of Scotland Society*. Dinner in the Students' Union.
Information: Dr D.G. Littlewood, Department of Anaesthetics, Royal Infirmary, Edinburgh EH3 9YW.

26 *Glasgow & West of Scotland Society*. Dr G.W. MacNab, Presidential Address.
Information: Dr D.S. Arthur, Royal Hospital for Sick Children, Glasgow G3 8SJ.

April 1986

7–25 *Faculty of Anaesthetists*, London. *Course on Anaesthetics* for Part 3 FFARCS.
Information: Courses Assistant, Faculty of Anaesthetists, 35/43 Lincoln's Inn Fields, London WC2A 3PN.

8–10 *Junior Anaesthetists' Group*. AGM and Annual Scientific Meeting at Cardiff.
Information: Association of Anaesthetists, 9 Bedford Square, London WC1 3JH.

8–9 *West Midlands Intensive Care Group*. 6th Annual Meeting at Wyddrington Hall.
Guest Speaker: Dr Margaret Branthwaite.
Information: Miss M.C. Wood, Postgraduate Medical Centre, East Birmingham Hospital, Birmingham B9 5ST.

8–9 *Blood Flow Group, Biological Engineering Society*. Obstetric & Neonatal Blood Flow. KCH.
Information: Biological Engineering Society, Royal College of Surgeons, 35/43 Lincoln's Inn Fields, London WC2A 3PN.

9 *Sheffield Anaesthetists*. Dr J.F. Nunn.
Information: Dr N.R. Bennett, Department of Anaesthetics, Royal Hallamshire Hospital, Sheffield S10 2RX.

9 *Northern Ireland Society*. AGM and Dr D.L. Coppell, *High frequency ventilation* (film).
Information: Dr J.E. Hegarty, Department of Anaesthetics, 97 Lisburn Road, Belfast BT9 7BL.

9 *Reading Anaesthetists*. Title to be announced.
Information: Dr A. Marshall Barr, Department of Anaesthetics, Royal Berkshire Hospital, Reading RG1 5AN.

11 – 12 *Intensive Care Society*. Spring Meeting at Newcastle upon Tyne.
Information: Dr D.W. Ryan, Freeman Hospital, Newcastle upon Tyne NE7 7DN.

11–12 *Anaesthetic Research Society* at Leeds.
Information: Dr A.R. Aitkenhead, University Department of Anaesthetics, Leicester Royal Infirmary, Leicester LE1 5WW.

16 *FFARCS Pt 2 papers*, London.

17 *FFARCS Pt 3 applications due*, London.

17 *Manchester Medical Society, Section of Anaesthetics*. Out of Town Meeting, Lancaster Royal Infirmary. *Symposium* on Pain Relief, Dr A. Kilpatrick, *Acupuncture*.
Host: Dr M.A. Rucklidge, Department of Anaesthetics, Lancaster Royal Infirmary, Lancaster LA1 4RP.
Information: Dr E.E.M. Thompson, University of Manchester, Oxford Road, Manchester M13 9PL.

18 *Section of Anaesthetics, Royal Society of Medicine*. Prof. M.J. Cousins (Flinders Univ.), *Hepatotoxicity of halothane: an enigma of drug toxicity*.
Information: Sections Office, Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE.

19 *North of England Society*. Symposium: Title to be announced.
Information: Dr J.E. Charlton, Department of Anaesthetics, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP.

22 *Glasgow & West of Scotland Society of Anaesthetists*. AGM.
Information: Dr D.S. Arthur, Royal Hospital for Sick Children, Glasgow G3 8SJ.

25–27 *Scottish Society of Anaesthetists*. Annual Meeting at Peebles Hotel Hydro.
Information: Dr W.F.D. Hamilton, Department of Anaesthesia, Ninewells Hospital, Dundee DD2 9SY.

28 *Wessex Anaesthetic Club.* Prof. W.S. Nimmo, *New directions in the administration of analgesics after surgery.*

Information: Dr D.V. Rutter, Shackleton Department of Anaesthetics, Southampton General Hospital, Southampton SO9 4XY.

International congress calendar

1986

17–20 January. Long Beach, California. *2nd Anaesthesia and the Law Symposium.*

Information: The Ohio State University Hospital, Department of Anesthesiology, 410 West 10th Avenue, Columbus, Ohio 43210, USA.

27–30 January. Florida.. *Medical Management of the Surgical Patient.*

Information: Catherine Sentman, Program Coordinator, Office of Continuing Education, Turner 22, 720 Rutland Avenue, Baltimore MD 21205, USA.

1–2 February. Nagpur, India. *Second Annual Conference of the Indian Society for Study of Pain.*

Information: Dr S. Shrirao, Organising Secretary, Choti Dhantoli, Nagpur 440012, India.

1–8 February. Vail, Colorado. *12th Annual Vail Conference in Anesthesiology.*

Information: Professional Seminars, PO Box 012318, Miami, Fl. 33101, USA.

5–7 February. Groningen, The Netherlands. *International symposium on, The intensive care unit—A cost-benefit analysis.*

Information: Dr D.R. Miranda, Director, ICU, University Hospital, Groningen, The Netherlands.

5–8 February. Melbourne, Australia. *8th annual Scientific Meeting of Australian Pain Society.*

Information: Dr T.F. Little, Pain Management Centre, Royal Southern Memorial Hospital, 260 Kooyong Road, Caulfield 3162, Victoria, Australia.

8–15 February. Vail, Colorado. *Vail Symposium in Intensive Care.*

Information: Professional Seminars, PO Box 012318, Miami, Florida 33101, USA.

9–13 February. Waikiki, Hawaii. *14th Obstetric Anesthesia Conference.*

Information: The Ohio State University Hospital, Department of Anesthesiology, 410 West 10th Avenue, Columbus, Ohio 43210, USA.

14–15 March. Basel, Switzerland. *Anaesthesia and Intensive Care for Infants and Children. 6th Myron B. Laver International Postgraduate Course.*

Information: Secretariat, Department of Anaesthesia. University of Basel/Kantonsspital, CH-4031 Basel, Switzerland.

15–19 March. Las Vegas, Nevada. *60th Congress of the International Anesthesia Research Society.*

Information: Emerson A. Moffitt, MD, International Anesthesia Research Society, 3645 Warrensville Center Road, Cleveland, Ohio 44122, USA.

15–22 March. Flims, Switzerland. *7th International Symposium on anaesthesia, reanimation and intensive care.*

Information: Prof. Dr Ingrid Podlesch, Universitats-Klinik für Kiefer und Plastische Gesichtschirurgie, Moorenstrasse 5, D-4000 Düsseldorf, Germany.

17–20 March. Vail, Colorado. *6th Medical Monitoring Technology Conference.*

Information: The Ohio State University Hospital, Department of Anesthesiology, 410 West 10th Avenue, Columbus, Ohio 43210, USA.

23–27 March. Cape Town. *South African Society of Anaesthetists.*

Information: Dr Roger E. Thornington, 1986 SASA Congress, Department of Anaesthetics, Medical School, Observatory 7925, South Africa.

23–28 March. Vail, Colorado. *13th Neonatal and Infant Respiratory Symposium.*

Information: The Ohio State University Hospital, Department of Anesthesiology, 410 West 10th Avenue, Columbus, Ohio 43210, USA.

15–18 April. Brussels. *Sixth International Symposium on Intensive Care and Emergency medicine.*

Information: Dr J.L. Vincent, Department of Intensive Care, Erasmus University Hospital, Route de Lennik 808, 1070 Brussels, Belgium.

26–30 May. Washington, DC. *Annual Meeting American Society of Critical Care Medicine.*

Information: SSCM, 223E, Imperial Way, Suite 110, Fullerton, CA 92635, USA.

28 May–3 June. Gothenburg and Stockholm. *Association of Paediatric Anaesthetists and Swedish Society of Anaesthetists Joint Congress on Paediatric Anaesthesia and Intensive Care.*

Information: Dr B. Ekstrom Jodal, Anestesiavdelning, Ostrajukhuset, Gothenburg, Sweden.

11–14 June. Hamburg. *3rd European Congress on Intensive Care Medicine.*

Information: Hamburg Messe und Congress, GmbH, Postfach 30 24 80, D-2000, Hamburg 36, Fed. Rep. Germany.

14–21 June. Cannes, France. *American and European Views on Critical Care.*

Information: N.W. Brian Craythorne, Department of Anesthesiology, PO Box 016370, Miami, Florida 33101, USA.

19–22 June. Barcelona, Spain. *8th Annual Meeting of European Academy of Anaesthesiology.*

Information: Prof. M.A. Nalda-Felipe, Department of Anesthesiology, Hospital Clinico, Facultad de Medicina, Villarroel 170, 08036 Barcelona, Spain.

24–27 June. Dublin. *Third European Congress of Obstetric Anaesthesia and Analgesia.*

Information: Congresses and Expositions Ltd, 44 Northumberland Road, Dublin 4, Ireland.

27–30 August. Rotterdam, The Netherlands. *First European Congress of Paediatric Anaesthesia.*

Information: Dr H.J. Manschot, Department of Anesthesiology, Sophia Children's Hospital, Gordelweg 160, 3038 GE Rotterdam, The Netherlands.

2–6 September. Malmo, Sweden. *Fifth Congress of the European Congress of Regional Anaesthesia.*

Information: Anestesikliniken, Malmo Allmanna Sjukhus, S 21401 Malmo, Sweden.

3–6 September. Rotterdam, The Netherlands. *Fourth International Symposium on Computing in Anaesthesia and Intensive Care.*

Information: Omar Prakash, MD, Thorax Centrum, PO Box 1738 3000 DR Rotterdam, The Netherlands.

7–13 September. Vienna. *7th European Congress of Anaesthesiology.*

Information: Professor K. Steinbereithner, Spitalgasse 23, A-1090 Vienna, Austria.

16–19 September. Haifa, Israel. *14th International Congress of the Israel Society of Anesthesiologists.*

Information: Congress Secretary, PO Box 50006, Tel Aviv 61500, Israel.

18–19 September. London, England. *Annual Scientific Meeting of the Association of Anaesthetists of Great Britain and Ireland.*

Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9, Bedford Square, London, WC1 B3RA.

27–30 November. Grenoble, France. *4th International Conference on Disaster Medicine.*

Information: Ste Intern, Medecine de Catastrope, PO Box 59, CH 1213, Petit Lancy 2, France.

1987

7–9 May. Paris. *VI Annual Meeting of the European Society of Regional Anaesthesia.*

Information: MAPAR, Departement d'Anesthesiologie, Hopital de Bicetre, 94270 Kremlin-Bicetre, France.

20–23 July. London, England. *2nd International Symposium on The History of Anaesthesia.*

Information: Secretariat. A Symposium on the History of Anaesthesia, Association of Anaesthetists of Great Britain and Ireland, 9, Bedford Square, London, WC1B 3RA.

23–25 July. Oxford, England. 50th anniversary of the founding of the Nuffield Department of Anaesthetics.

Information: Nuffield Department of Anaesthetics, Department GP/87, Radcliffe Infirmary, Oxford OX2 6HE.

2–7 August. Hamburg, West Germany. *Vth World Congress on Pain.*

Information: Vth World Congress on Pain, c/o Hamburg Messe und Congress GmbH, Congress Organization, Postfach 30 24 80, 2000 Hamburg 36, West Germany.

10–11 September. Sheffield, England. *Annual Scientific Meeting of the Association of Anaesthetists of Great Britain and Ireland.*

Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9, Bedford Square, London, WC1B 3RA.

1988

22–28 May. Washington, DC. *9th World Congress of Anaesthesiology.*

Information: American Society of Anesthesiologists, 515 Busse Highway, Park Ridge, Illinois 60068, USA.

15–16 September. Southampton, England. *Annual Scientific Meeting of the Association of Anaestheists of Great Britain and Ireland.*

Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9, Bedford Square, London WC1B 3RA.

Anaesthesia, 1986, Volume 41, pages 120–127

Association of Anaesthetists of Great Britain and Ireland

Annual Report of Council 1984–1985

1. Membership of the Association

The total membership of the Association is 5257 (5011).

Honorary	29	(27)
Ordinary	2186	(2215)
Junior	1719	(1539)
Corresponding	35	(36)
Overseas	991	(917)
Retired	264	(242)
Senior	19	(20)
Associate	14	(15)

(Last year's figures in brackets.)

There were 46 resignations during the year.

Deaths

Council records with regret the death of the following members:

Anning, R. (*Harrogate*), Ball, H. (*Ringwood*), Belsham, Brig. W.F. (*Kent*), Berney, Jill (*Suffolk*), Blazeby, H. (*Canterbury*), Bretherton, K.W. (*S. Africa*), Clayton, R.B. (*Bucks.*), Coleman, E.R. (*London*), Cuthbert, T.D. (*Manchester*), Frost, J.L. (*Plymouth*), Hawksley, Margaret (*Wilts.*), King, R. (*Sheffield*), McDowall, D.G. (*Leeds*), McErvel, C. (*Belfast*), McVey, A. (*Newcastle, Staffs.*), Miller, A.G. (*Helensburgh*), Odell, J.R. (*Hampshire*), Ordish, Pamela (*Warks.*), Scriven, W.H. (*Surrey*), Steele, G.C. (*London*), Tracey, R.A.J. (*Newry*).

2. John Snow Silver Medal

Council recommended the award of the John Snow Silver Medal to:

Professor T.J. Gilmartin, Professor of Anaesthesia, Dublin.

3. Honorary Membership

Council recommended for election to Honorary Membership:

Dr G. Jackson Rees. Consultant Anaesthetist, Alder Hey Children's Hospital, Liverpool. For distinguished services to paediatric anaesthesia.

4. Pask Certificates of Honour

Council recommended the award of Pask Certificates to:

Prof. Dr Med. Deitrich F. Kettler (*Gottingen*), Prof. Dr Med. Horst O. Stöeckel (*Bonn*), Dr W. Maurice Brown (*Belfast*), Dr Margaret L. Heath (*London*), Cyril Jones Esq., Senior Operating Department Assistant (*East Grinstead*).

5. Annual Scientific Meeting of the Association—Exeter 20–21 September 1984

The Annual Scientific Meeting was held in the Great Hall of the University of Exeter. A full scientific and social programme had been organised by the local Committee of Exeter anaesthetists. There were some 500 registrants. The John Snow Lecture 'Today's Pollution of the Parish Pump', was delivered by Dr Michael O'Donnell, medical writer and broadcaster.

A candlelit concert in Exeter Cathedral by the Academy of St Martin's in the Fields, was particularly memorable.

The Annual Dinner was also held in the University in the company of many distinguished guests.

6. Annual General Meeting 1984

This was held in the Great Hall of Exeter University on Friday, 21 September 1984 with the President, Professor M.D. Vickers, in the Chair. Over 150 members were present.

Honorary Membership was conferred on Professor H. Lehmann, Professor Emeritus of Clinical Chemistry, University of Cambridge. Dr W.D. Wylie, Past President of the Association was unanimously elected to Honorary Membership. Dr C.F. Scurr, CBE, MVO, was awarded the John Snow Silver Medal. Pask Certificates were awarded to Dr Patricia Coyle, Uganda, Dr W.D.A. Smith, OBE, (*Leeds*), and Dr H. Grant-Whyte, (*South Africa*).

The Minutes of the Meeting have been circulated to all members.

7. Linkman Conference 1984

The Ninth Annual Linkman Conference was held on 19 September 1984 with the President in the Chair. Information was given to Linkmen about the purchase of, and appeal for, 9 Bedford Square, and a lively discussion ensued. Other topics covered by the Conference were 'Workload of Consultants in Hospitals with reduced Junior staff', 'Anaesthesia in isolated situations in the UK', 'References in the NHS', 'Mortality' and 'Study Leave'.

A detailed report of the Conference has been circulated to Linkman and published in *Anaesthesia*.

8. Administration for Anaesthetists

A one-day course for anaesthetists on administration was held on 12 January 1985 at the Royal College of Surgeons. It was attended by about 140, mainly younger consultants and senior registrars. Topics covered the work of the Faculty and the Association—the Regional Committees—and the needs and organisation of the departments of anaesthetics in the District General Hospital.

9. Joint Scientific Meeting with the German Society of Anaesthetists—Bonn, 15/19 May 1985

A most successful joint meeting of members of this Association and the German Society of Anaesthetists was held in Bonn on 16 and 17 May 1985. The scientific sessions were held with two-way simultaneous translation, and covered a wide range of British and German views on current topics of anaesthesia and intensive care. There were about 300 German delegates and about 100 from the UK.

Professor H. Stoeckel, the local organiser, and Professor F. Kettler, President of the German Society were awarded Pask Certificates. Dr T.B. Boulton, President, Professor G. Smith, Joint organiser of the Scientific Programme and Dr M.T. Inman, Honorary Secretary, were made Corresponding Members of the German Society.

An excellent social programme was completed by a memorable day on the Rhine.

10. Future meetings

Association Meetings

1985—Postgraduate Study Day, *19 October 1985*, Royal College of Surgeons.

1986—Junior Anaesthetists' Group Linkman Conference and Annual Scientific Meeting *8/10 April 1986*, Cardiff.

—Association Linkman Conference, *17 September 1986*, London.

—Annual Scientific Meeting & Exhibition, *18/19 September 1986*, City University, London.

1987—Junior Anaesthetists' Group Linkman Conference and Annual Scientific Meeting, *March/April 1987*, Belfast.

—Association Linkman Conference, *9 September 1987*, Sheffield.

—Annual Scientific Meeting & Exhibition, *10/11 September 1987*, Sheffield.

1988—Junior Anaesthetists' Group Linkman Conference and Annual Scientific Meeting, *March/April 1988*, Nottingham.

—Association Linkman Conference, *14 September 1988*, Southampton.

—Annual Scientific Meeting & Exhibition, *15/16 September 1988*, Southampton.

Sponsored Meetings

1987—2nd International Symposium on the History of Anaesthesia, *20/23 July 1987*, London.

Other Meetings

1986—7th European Congress of Anaesthesiology (WFSA), *7/13 September 1986*, Vienna.

—7th Asian/Australasian Congress of Anaesthesiology (WFSA), *20/25 September 1986*, Hong Kong.

1988—9th World Congress of Anaesthetists (WFSA), *22/28 May 1988*, Washington, DC.

11. Council

During the year October 1984–September 1985, Council and its Advisory Committee have each met on four occasions. The attendance of members at Council and its subcommittees and working parties is shown in Appendix A.

Council wishes to express its appreciation of the work done in its offices by Miss Ann Muir, Administrative Secretary, by Mrs Betty Tyler, her assistant, and by Miss Pat Plant, the Financial Assistant. The contribution of our Financial Adviser, Mr Ernest Warburton, continues to be most beneficial and Council are very grateful to him for his extensive and purely voluntary efforts.

Retiring from Council this year will be Dr W.R. MacRae, who, as Honorary Secretary, has worked extremely hard for the Association, and has made a particular contribution with the installation of a computer system for the membership list and a word-processor for the records of the Association. Both he and Dr Jean Horton have been proposed as Vice-Presidents of the Association.

Four elected members of Council retire after serving for four years. Dr E.A. Cooper, Dr J.M. Lawson, Dr J.M. Leigh and Dr J.S. Crawford. All have served Council in many ways on its working parties and subcommittees have earned Council's gratitude.

(i) *Premises for the Association.* Three subcommittees have been set up to be responsible to Council for the development of 9 Bedford Square, a Fund Raising Committee, a House Committee and a Furnishing Working Party. The House Committee is charged with commissioning 9 Bedford Square and the subsequent maintenance and management of the fabric furnishing and function of the new Headquarters of the Association. The Furnishing Working Party has been formed to deal with the initial task of choosing and obtaining furniture uner the Chairmanship of Dr M. Rosen, who is also Chairman of the Appeals Committee.

The extensive renovations to the listed building under the direction of the architects, Shankland Cox, will be completed by the end of September 1985, and it is proposed that the Secretariat will transfer to Bedford Square in late October or early November 1985. The postal address of the Association from 1st December 1985 will then be *9 Bedford Square, London WC1B 3RA and the telephone number (01) 631 1650.* The lease of the present suite in Tavistock House runs until the end of the year; the overlap will facilitate an easy transfer.

The General Office, the adjacent Reception Area and the Hall will be fully furnished by the time the Secretariat moves. The rest of the building will be curtained and carpeted and the present furniture from Tavistock House will be put to use in the Committee Room and other working offices. Furniture will be carefully selected and purchased for the principal public rooms, including the Members' Room and the Council Room during 1986. Council is profoundly grateful for offers of furniture from a number of societies, departments of anaesthesia and other organisations connected with anaesthesia, in addition to individual donors. We particularly wish to express thanks to the *British Journal of Anaesthesia* who have donated the furnishing of the Library, to the Obstetric Anaesthetists' Association for the gift of a beautiful sculpture by Jonah Jones for the Reception Area, and to the Australian Society of Anaesthetists for the offer of a contemporary Australian painting.

The Official Opening Ceremony will take place in the Spring of 1987. A Working Party charged with the task of organising this event has been formed under the Chairmanship of Dr M. Rosen, the nominee of Council for the office of President for 1986/88.

(ii) *Postgraduate Study Day.* Using the same successful formula, the Association has again collaborated with the Faculty of Anaesthetists for a Postgraduate Study Day. Some 500 anaesthetists attended the Royal College of Surgeons, at which 18 lectures were delivered.

12. Linkman Organisation

The Linkman organisation remains a most useful method of communication with each and every Department of Anaesthetics. Following last year's Conference attended by some 140 Linkmen, it was stressed that we would like to achieved one representative from each department at the Conference. The next date was given and deputies are encouraged to attend if the Linkman is unable to come.

Council have prepared a proforma and guidelines for References in the NHS which are available on request.

Many individual matters are dealt with by letter and telephone from the Linkmen to the Secretariat and Honorary Secretary.

13. Research and Education Committee

The annual budget of this committee (Chairman, Dr E.A. Cooper) is of the order of £30 000–£35 000. It is important that in this year of purchase and refurbishment of 9 Bedford Square, Council has agreed that there will be no reduction of expenditure for purposes of research and education.

Dr Fiona McLennan has resigned from the Association's Research Fellowship. An advertisement for the next Fellowship will appear shortly. During this last year four out of seven applications for Travel Grants were successful. Five out of six requests for Research Grants were also met wholly or in part.

According to the current regulations, travel grants are limited to £250 and are not given to people going overseas to take up employment. The committee has made proposals for a review of the current limit and the creation of another type of award to provide financial help to members who are going overseas to take up a clinical or teaching post in developing countries.

14. Safety Committee

The Safety Committee (Chairman, Dr P.W. Thompson) met on 27 July 1984 and 15 March 1985. Major items which have been discussed and resolved satisfactorily included the future of servicing arrangements for TEC II vaporizers and Boyle anaesthetic machines, types G, H, K and L, and future plans for the continuation of the DHSS's evaluation reports.

The committee noted with genuine satisfaction the establishment by the British Standards Institution of a Health Care Committee to 'control the working of the technical committees in the Health Care Industry and to take such action as may be considered appropriate for furthering standardisation'. This is leading to a great improvement in the coordination of performance, general safety and electrical safety requirements.

A further matter of considerable importance is the question of earth-free power supplies and double-pole fusing etc. in operating theatres; discussion on this matter is being continued at the committee's next meeting.

15. International Relations Committee

The International Relations Committee (Chairman, R.J. Eltringham) met on two occasions during the past year, directing much of its attention to the training of anaesthetists in developing countries and, in particular, to helping them to become self-reliant. Our outstanding commitments were, in the most part, fulfilled and, in addition, several new enterprises were undertaken.

Dr Inman returned to Nepal early in 1985 to deliver a training course in anaesthesia to government-sponsored medical officers in and around Kathmandu. He was joined by a technician from Plymouth who was able to advise on the purchase, maintenance and servicing of apparatus. The anaesthetic service there is continuing to develop slowly and a local D.A. examination has now been established, but further visits will be required if momentum is to be maintained.

The benefit of helping developing countries to become self-sufficient in anaesthesia training is well illustrated by the situation in the Sudan. The British Council sponsored training link between the Universities of Bristol and Khartoum continues to flourish. The status of anaesthesia in the medical community there has clearly been enhanced and local graduates of high calibre are beginning to emerge. In the recent Mastership examination, seven out of eight candidates were successful and our thanks are due to Dr A. Black and his colleagues from Bristol for their great efforts in helping achieve this satisfactory state of affairs.

We have been successful in obtaining help for the Department of Anaesthesia at the University of Lusaka in Zambia. Dr R. Sinclair is due to commence a one year appointment as Senior Lecturer in 1985, top-up financial support coming from the British Council and the Research and Education Committee. It is hoped to repeat this annually, and suitable lecturers to succeed Dr Sinclair are being sought.

Efforts to send a lecturer to Uganda to assist Dr Patricia Coyle have so far proved unsuccessful. Arrangements were well advanced for Dr Lavelle to undertake this assignment for a year, but these were thwarted by administrative and political considerations. Our efforts continue to find a suitable deputy. Meanwhile, Dr Lavelle has gone to Ethiopia where his expertise is sorely needed.

The visit of Dr Hōrning as part of the cultural agreement with the German Democratic Republic was scheduled for early 1985. This was postponed at her request, but will take place later in the year, to be followed by further British visits to the German Democratic Republic.

During the past year, additional requests for help with training programmes have been received from the Universities of Kumasi (Ghana) and Harare (Zimbabwe), and a positive response to these challenges is planned. It is gratifying to note that there seems to be an ever-increasing demand for the services of British-trained anaesthetists throughout the world, and the next year promises to be one of great activity.

16. Editorial Board

The Editorial Board (Chairman, Dr P.J. Helliwell) met on two occasions. The contract with our publishers became due for renegotiation and possible renewal by 1 January 1985. Tenders were received from other publishing houses, but, after full enquiry, it was decided that a further period of four years should be agreed between ourselves and Academic Press. This agreement was signed in October 1984 to commence on 1 January 1986.

There have been several changes in staff at Academic Press, and the Board would like to record their thanks to Miss Jenny Bruce (advertising), whose place has been taken by Miss Joy Clarke. Miss Jackie Jones, our technical subeditor at Academic Press, has left the firm and her place has been taken by Dr Sue Silver.

Dr Aileen K. Adams, elected member of the Board, has retired after a number of years of valuable service.

Dr I.M. Corall (Kings), completed a period of service as assistant editor, for which the Board is grateful. The Board is pleased to welcome Dr R.M. Jones (Guy's), who has taken his place.

17. Finance Committee

The Finance Committee (Chairman, Dr M. Rosen) has continued to oversee the finances of the Association during 1984/85. Having held the subscription rate last year, it was now recognised that it was going to be necessary to propose to the AGM that the rate for Ordinary members will be £60 p.a.

Funding of 9 Bedford Square has required a planned realisation of investments and this has proceeded in line with previous projections. Consideration has been given to the future distribution of finance within the Association in view of the many educational, safety and research activities of departments of the Association, and a charitable company will replace the Research and Education Trust.

18. Private Practice Committee

During the year, the Private Practice Committee (Chairman, Dr M.T. Inman) has been in discussion with BUPA. Topics have included the level of the anaesthetic fees for general anaesthesia and for special procedures in chronic pain work. It was estimated by the committee, that the guidelines published by the Association would have been held for 2 years, and that in January 1986, rises broadly in line with inflation would probably be recommended. This was noted by BUPA, who have indicated that difficulties in separating benefit still remain. A considerable number of queries regarding the conduct of private practice and the setting up of group practice schemes are received.

19. Junior Anaesthetists' Group

The JAG group (Chairman, Dr Wendy Scott) has continued to grow in numbers and in political awareness over the past year. The total number of Juniors now stands at 1720.

The Annual Scientific Meeting was held this year in Manchester at the end of March. It was a good meeting and the local organising committee is to be commended for its work in arranging such an excellent scientific and social programme. The standard of papers for the Registrar's Prize was even higher than in previous years. 'Ohmeda' has kindly agreed to sponsor this prize for 5 years in the first instance.

The JAG Committee welcomed three new members elected at the 18th Annual General Meeting on 29 March 1985 in Manchester.

Practically, the JAG Committee has produced The Career Guide issued in September 1984 which replaced an earlier Career Guide produced by this committee. This was mainly the work of Dr P. Bickford Smith and Dr T.B. Boulton.

Dr W. Hamlin sent out a questionnaire to all Senior Registrars concerned with job conditions and change in on-call patterns. The results of this questionnaire were presented at the AGM. Dr Hamlin is to be congratulated on his work and excellent presentation. It is hoped that these results will be published.

Dr A. Nicholl, together with Dr T.B. Boulton and 'Ohmeda', has produced new display material for exhibition at Careers Fairs. This is aimed mainly at medical students and has already been seen in Cardiff and Manchester.

The main achievement over the past year is the establishment of a Junior Linkman network. The first Junior Linkman Conference was held in Manchester on the morning of the start of the Annual Scientific Meeting. Dr Nicholl is the Junior Linkman Coordinator and has already sent out his first Junior Linkman Newsletter.

The JAG Committee welcomes the opportunity the Junior Linkman Scheme will provide to hear the views of its members, and will be better able, in the future, to represent these views to Council.

There was a meeting for Doctors with Domestic Commitments held in Reading on 15 June 1985. The idea and some of the organisation was done by the JAG Committee. It was a useful meeting, attended by eighty people.

The numbers of Committees of Council and other Committees on which there is now Junior representation has increased. The Juniors welcome this and try to provide constructive input and to represent their Junior colleagues.

The JAG Committee acknowledges with gratitude, the continued support and help it has from Council's representative, Dr T.B. Boulton.

20. Confidential Enquiry into Peri-operative Deaths

Considerable progress has been made on this combined study between the Association of Anaesthetists of Great Britain and Ireland and the Association of Surgeons of Great Britain and Ireland. The protocol was published in November 1984, with widespread support from very many clinical institutions, including the Royal Colleges of Surgeons, Obstetricians and Gynaecologists. Physicians and the Faculties of Anaesthetists and of Dental Surgery. A pilot study was started in three districts (Exeter, Darlington and the Middlesex Hospital), and good responses have been achieved. Meanwhile, the three clinical coordinators have travelled to many individual hospitals in the three regions to be studied (South Western, Northern and North East Thames), with the intention that every district shall be visited before the start of the study. There is considerable interest and enthusiasm for the venture, although individual reservations are, of course, to be respected.

Assessors, nominated by supporting bodies and other organisations, have been briefed at a series of meetings and the questionnaire has been reviewed and revised in the light of comments. More than 200 individuals have agreed to take part as assessors and their names will be published shortly.

The working party has met on two occasions to oversee the activities of the coordinators, and has approved the final design of the questionnaire, whilst recognising that it is unlikely to satisfy all participants. Supplementary notes to the protocol have been published. Professor I. McColl has resigned from the working party and his place has been taken by Professor A. Johnson (*Sheffield*).

21. Working Parties

Specialist Anaesthetic Societies. A meeting with the Specialist Societies in Anaesthesia and Intensive Care, was held in November 1984. The meeting was attended by a representative of the newly formed Society of Cardiothoracic Anaesthetists. Problems of mutual interest, including dates of meetings and communication were discussed.

References in the NHS. During the year, the Working Party on References in the National Health Service has published its code of good practice, and a proforma for any members who wish to use them. These are avilable at the Association offices.

Recovery Facilities. The Working Party met several times during the year and has prepared a document on recovery facilities. The document contains advice on basic recovery facilities, the purpose-built recovery room and on the training of recovery room staff. It is designed to assist members to improve their own recovery facilities and meet the up-dated requirements of the Hospitals Recognition Committee. The document will be available shortly from the Association offices.

Hospital Visiting. A request has been received from the Junior Anaesthetists' Group for the Association to issue guidelines to candidates for posts at all levels on the question of hospital visiting both before and after the short-listing procedure.

A Working Party has been set up to consider the preparation of a Code of Good Practice on this subject. Following the first meeting of this Working Party, letters were sent to all Linkmen and the problem will be discussed in the Open Forum of the forthcoming Linkman Conference on 11 September, prior to the next meeting of the Working Party.

2nd International Symposium on the History of Anaesthesia—1987. The Symposium will be sponsored by the Association. It will be held at the Royal College of Surgeons of England, Lincoln's Inn Fields, London WC2, from 20/23 July 1987.

The Organising Committee is under the Chairmanship of Dr T.B. Boulton. Dr M. Rosen is Honorary Treasurer, Dr P. Baskett, Secretary-General and Dr P.J.F. Thompson, Dr R.H. Ellis and Dr R.S. Vaughan are responsible for the Scientific Programme, the Social Events and the Technical Exhibition respectively.

Plans for the Symposium are now well advanced in all areas and there has been considerable support from overseas. The principal task of the Committee in the year ahead will be one of active promotion in preparation for the receipt of initial registrations early in 1987. The Organising Committee looks forward to support from the Society for the Study of the History of Anaesthesia, which is to hold its inaugural meeting during the 1985 Annual Scientific Meeting.

22. Monospecialist Committee for Anaesthesia and Resuscitation of the European Union of Medical Specialists (UEMS)

The Anaesthetic Monospecialist Committee of the UEMS has met in October 1984 in Paris, and in May 1985 in Bonn.

Dr D.C. Howat is President of the Committee until May 1986 and will be succeeded by Dr Baskett for the period 1986/88. The Committee has produced guidelines for the basic facilities and equipment required for the administration of anaesthesia in hospitals in the EEC, which was prepared by Dr Baskett.

There is continued concern at the revision of the training arrangements in France, which have been dictated by the French Government and representations are being made to the UEMS Commission concerning this matter. The problem also applies to other specialties, apart from anaesthesia. The numbers of trained anaesthetists and anaesthetists in training in each country continues to be monitored, and there is evidence of unemployment in certain EEC countries amongst anaesthetists. Efforts are being made to reduce the practice of nurses administering anaesthetics without supervision.

Future items for discussion will include: Intensive Care Training in the anaesthetic curriculum, the matter of examinations in anaesthesia in EEC countries, the position of the European Diploma in Anaesthesiology and the matter of assistance for anaesthetists.

23. Resuscitation Council

The Resuscitation Council continues to meet on a regular basis and membership is drawn from all specialties, with a legitimate interest in CPR.

A number of guideline publications have been produced. These include a Resuscitation Flip Chart and wall poster aimed at Basic Life Support. An Advanced Life Support poster has also been produced and all of these publications are available from the Honorary Secretary, Dr David Zideman, Department of Anaesthesia, Hammersmith Hospital, Ducane Road, London. The Council has also organised a multicentre study to assess the practice and results obtained from CPR in hospitals throughout the United Kingdom.

Representatives from the Council have attended the national meeting of the American Heart Association, who offer advice concerning the revised American Heart Association's standards for resuscitation.

A major public education exercise is planned for 1986, led by the BBC and other members of the media.

Composition of Council, its Sub-Committees and Working Parties

Council

Five meetings held (attendance in brackets).

Officers: Dr T.B. Boulton, President (5); Professor M.D. Vickers, Immediate Past President (2); Professor J.P. Payne, Vice-President (5); Dr M. Rosen, Vice-President (5); Dr M.M. Burrows, Honorary Treasurer (5); Dr M.T. Inman, Honorary Secretary (4); Dr W.R. MacRae, Immediate Past Honorary Secretary (4); Dr J.N. Lunn, Editor (3).

Elected Members: Professor A.P. Adams (4); Dr Elizabeth Bradshaw (2); (working abroad); Dr E.A. Cooper (5); Dr R.J. Eltringham (5); Dr J.S. Crawford (3); Dr W.H.K. Haslett (5); Dr D.J. Hatch (4); Dr J.M. Leigh (3); Dr J.I.M. Lawson (4); Dr P. Morris (5); Dr T.W. Ogg (4); Dr J.F. Searle (4); Professor G. Smith (4); Dr W.S. Wren (2); Dr Wendy Scott (4); Dr W. Hamlin (1) (From Feb. 85).

Co-opted Members: Dr P.J.F. Baskett, Dr G.W. Black, Professor D. Campbell, Dr E.B. Lewis, Dr P.J. Helliwell, Colonel J. McEwan, Professor C.M. Conway, Dr P.W. Thompson, Dr J.S.M. Zorab.

Advisory Committee

Four meetings held (attendance in brackets).

Chairman: Dr T.B. Boulton (4); Professor M.D. Vickers (2); Dr M. Rosen (3); Dr M.M. Burrows (1); Dr W.R. MacRae (4); Dr M.T. Inman (3); Dr J.N. Lunn (3); Dr P. Morris (4); Professor D. Campbell (–); Dr Wendy Scott (3).

Editorial Board

Editor Emeritus: Dr C. Langton Hewer; *Chairman:* Dr P.J. Helliwell; *Editor:* Dr J.N. Lunn; *Advisory Editors:* Dr R.S. Atkinson; Dr T.B. Boulton; *Assistant Editors:* Dr C.E. Blogg; Dr R. Greenbaum; Dr R.M. Jones; Dr M. Morgan. *Other Members:* Dr P.J.F. Baskett, Dr C.F. Scurr, Dr Jean Lumley (Council Representative), Dr Lauren Allan (JAG). *Co-opted Members:* Mr E. Warburton (Financial Adviser); Mrs Joan Fujimoto (Academic Press); Dr Sue Silver (Academic Press); Miss Jackie Jones (Academic Press); Mrs S.M. Campbell (Editorial Assistant).

Finance Committee

Dr M. Rosen (*Chairman*); Dr E.A. Cooper; Dr W. Haslett; Dr J.I.M. Lawson; Dr P. Morris; Dr J.F. Searle; Mr E. Warburton.

Safety Committee

Dr P.W. Thompson (*Chairman*); Professor A.P. Adams; Dr Elizabeth Bradshaw; Dr D.J. Hatch; Dr T.W. Ogg; Dr S. Hill (JAG); Dr J. Bushman; Professor J.P. Payne; Air Commodore A.J. Merrifield; Professor M.K. Sykes; Dr Kate Allsopp (MDU); Dr C.J. Orr (MPS). *Co-opted:* Mr L.W.M. Arrowsmith (DHSS); Mr C. Bray (DHSS); Mr M. Freeman (BAREMA).

Research and Education Committee

Dr E.A. Cooper (*Chairman*); Dr Jean Lumley; Dr J.S. Crawford; Dr J.M. Leigh; Dr P. Morris; Dr T.W. Ogg; Professor J.P. Payne; Professor G. Smith; Dr Wendy Scott (JAG).

Junior Anaesthetists' Group

Dr Wendy Scott (*Chairman*); Dr G.W. Hamlin (*Secretary*); Dr Lauren Allan; Dr Anne Blythe; Dr L.E. Conroy; Dr A.D.J. Nicholl; Dr Nancy Redfern; Dr Deborah Schill; Dr I. Woods. Representative of Council: Dr T.B. Boulton.

CCHMS

Dr M.T. Inman.

Anaesthetists' Sub-committee of the CCHMS

Dr M.T. Inman (*Chairman*); Dr T.B. Boulton, Dr W.H.K. Haslet; Dr P. Morris; Dr A.D.J. Nicholl.

International Relations Committee

Dr R.J. Eltringham (Chairman); Dr Aileen K. Adams; Professor A.P. Adams; Dr Elizabeth Bradshaw; Dr D.J. Hatch; Dr W.S. Wren; Dr J.S.M. Zorab; Dr Wendy Scott.

By invitation representatives from: Appropriate Health Resources and Technologies Action Group; British Council; Inter-University Council; Bureau for Overseas Medical Services; Overseas Development Administration: World Federation of Society of Anaesthesiologists; Committee for International Cooperation in Higher Education.

Confidential Enquiry into Peri-operative Deaths

Professor M.D. Vickers (*Chairman*); Mr P. Bevan; Dr M.M. Burrows; Mr J. Craven; Mr B. Devlin; Mr D. Harper; Dr M.T. Inman; Professor J. Lumley; Dr J.N. Lunn; Professor A.G. Johnson; Dr P. Morris; Dr D.B. Scott.

Working Party on Morbidity in Anaesthesia

Dr J.M. Leigh (*Chairman*); Dr J.I.M. Lawson; Dr Jean Lumley; Dr M.E. Wilson; Dr T.W. Ogg; Dr M. Rosen; Dr J.N. Lunn.

Organising Committee of the 2nd International Symposium on the History of Anaesthesia

Dr T.B. Boulton (*Chairman*); Dr P.J.F. Baskett (*Secretary-General*); Dr M. Rosen (*Honorary Treasurer*); Dr R.S. Atkinson; Dr R.H. Ellis; Dr I. McLellan; Dr G.M.C. Paterson; Dr P.W. Thompson; Dr R.S. Vaughan; Dr D. Wilkinson; Dr J.S.M. Zorab.

Working Party on Recovery Facilities

Dr R.J. Eltringham (*Chairman*); Dr J.N. Horton; Dr W.H.K. Haslett; Dr P. Morris; Dr Elizabeth Bradshaw; Mrs J.S. Andrewes; Dr J.S.M. Zorab.

Meeting between the National Representative Bodies in Anaesthesia and the Specialist Organisations

Dr T.B. Boulton (*Chairman*); Professor A.P. Adams; Dr D.J. Hatch; Dr Aileen K. Adams; Dr G. Bush; Dr W. Fitch; Dr Constance Howie; Dr P. Morris; Dr Y.M.A. Tai; Dr G.J. Taylor; Dr T. Thomas; Dr R.D. Latimer; Dr Sheila Willatts.

The Officers of the Association are ex-officio members of all committees and working parties.

Faculty Advisory Panel on the Training of Anaesthetists: Dr G.W. Hamlin (JAG).

Liaison with BSI: Dr P.W. Thompson.

Joint Committee on Higher Training of Anaesthetists: Dr W.R. MacRae; Dr G.W. Hamlin (JAG).

EEC Monospecialist Sub-committee of the UEMS: Dr P.J.F. Baskett.

National Resuscitation Standards: Dr P.J.F. Baskett.

Manpower Advisory Panel (DHSS): Dr W.R. MacRae; Dr G.W. Hamlin (JAG).

Archives Working Party

T.B. Boulton (*Reading*) Honorary Archivist; D.J. Wilkinson (*London*) Honorary Curator; Charles King Collection of Historical Apparatus; I. McLellan (*Leicester*) Honorary Librarian. *Honorary Adviser on Technical Exhibitions:* R.S. Vaughan (*Cardiff*).

Anaesthesia, 1986, Volume 41, page 128

Stop Press

COURSES IN ANAESTHESIA

FFARCS Part I			
LEICESTER Department of Anaesthesia, Leicester Royal Infirmary	3–7 February 1986	NO FEE	Dr. D. Fell, Department of Anaesthesia, Leicester Royal Infirmary, Leicester, LE1 5WW

THIS PAGE CONCERNS YOU IF YOU ARE A MEDICALLY QUALIFIED ANAESTHETIST IN GREAT BRITAIN AND IRELAND, OVERSEAS OR IN TRAINING AND ARE NOT YET A MEMBER OF THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND OR IF YOU ARE A MEMBER OF ANOTHER PROFESSION WHO PRACTISES IN ANAESTHESIA AND YOU WISH TO APPLY FOR ASSOCIATE MEMBERSHIP

Ordinary Membership (*United Kingdom and Ireland only*)

Voting membership of the Association (the only effective body representing anaesthetists' interests in non-academic matters).

The right of attendance at the Annual General and Scientific Meetings and all other meetings of the Association of Anaesthetists.

Overseas and Associate Membership

The right of attendance at the Annual Scientific Meeting and other meetings of the Association.

Junior Membership (*United Kingdom and Ireland only*)

Voting membership of the Association.

Representation of the Council of the Association. The Chairman and Secretary of the Junior Group sit on Council as voting members.

Attendance at the Annual Scientific Meeting of the Association and at the special Annual Scientific Meeting of the Junior Anaesthetists' Group, at which Junior Members of the Association are given preference.

Membership Fees (inclusive of the journal *Anaesthesia*)

Ordinary Members: Entrance Fee **£5**, Subscription **£40** (Husband and wife **£60**)

Overseas and Associate Members: No Entrance Fee, Subscription **£40**

Junior Members: No Entrance Fee, Subscription **£20** (**£30** after 3 years if still in training)

Retired Members: who receive *Anaesthesia* **£7.50** (there is no subscription for those who do not)

How to apply for membership

Fill in the application form on the other side of this page.

Have it countersigned by two members of the Association, one of whom must be an Ordinary Member.

Tear out the page and send it to the address indicated overleaf.

Do not send money with your application

THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND

APPLICATION FOR MEMBERSHIP

to

The Association of Anaesthetists of Great Britain and Ireland
9 Bedford Square,
London WC1B 3RA, England

(This application will be considered by Council at its next meeting. NO MONEY should be sent in the meantime. After acceptance of the application by Council, the Hon. Secretary will notify the applicant of Council's decision and the amount of subscription payable in the current financial year.)

........................19

To the Honorary Secretary,
Association of Anaesthetists of Great Britain and Ireland

I (full name).. offer my name as a candidate

BLOCK LETTERS

for (a) MEMBERSHIP (b) OVERSEAS MEMBERSHIP (c) ASSOCIATE MEMBERSHIP (d) JUNIOR MEMBERSHIP of the Association (*please delete categories not applicable*)*

I hold the following appointment(s) as an anaesthetist (*please state grade if in the National Health Service, and indicate the approximate proportion of time spent in the practice of anaesthesia*):

....

....

....

Qualifications (with dates)..

....

(Signed)...

Address..

....Hospital Tel. No:.....................................

....Home Tel. No:..

We, being Members† of the Association, nominate as a candidate for MEMBERSHIP/OVERSEAS/ASSOCIATE/JUNIOR MEMBERSHIP

....

1. (Signed)..

(NAME IN BLOCK LETTERS)

Address..

BLOCK LETTERS

2. (Signed)..

(NAME IN BLOCK LETTERS)

Address..

BLOCK LETTERS

* See the reverse of this page for details of membership categories.

† One sponsor must be an Ordinary Member of the Assocation.

Notice to contributors to *Anaesthesia*

Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Articles accepted become copyright of *Anaesthesia*.

Contributors are requested to submit two copies of manuscripts. They are also advised to retain a third copy as the Editors cannot accept responsibility for the loss of manuscripts in the post. The covering letter should be signed personally by all the authors and careful consideration should be given to the decision to include more than five authors. Articles should be forwarded to:

Dr J. N. Lunn, Editor of ***Anaesthesia****, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.*

PREPARATION OF MANUSCRIPTS

Articles for *Anaesthesia* should be prepared in accordance with *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5) except that the titles of journals in the reference section should be given in full (see below). A reprint of these requirements of which this notice is a summary, can be obtained from the *British Medical Journal* price 50 pence (U.K.).

Type manuscripts on white bond paper, 20.3 × 26.7 cm or 21.6 × 27.9 cm (8 × 10½ in. or 8½ × 11 in.) or ISO A4 (212 × 297 mm) with margins of at least 2.5 cm (1 in.). Use double, and preferably triple, spacing throughout, including the references. Please do not use a dot matrix printer, particularly one with poor quality descenders or ascenders. Unseparated, fan-folded manuscripts may be returned to the author.

The manuscript should consist of the following sections in this order each beginning on a new page: *title page*, *summary* and *key words*, *text*, *acknowledgments*, *references*, *individual tables*, and *legends for figures*.

Number pages consecutively, beginning with the title page. Type the page number in the upper right-hand corner of each page.

THE TITLE PAGE

The name of the author and the address to which proofs and other correspondence is to be addressed should appear in the top left-hand corner of the sheet.

The main title should be restricted to five words if this is possible. It should be typed in capitals across the centre of the title page.

A subsidiary title of not more than 12 words may be supplied if this is considered to be necessary. This should be typed in lower case immediately beneath the main title.

The names of the authors should be typed IN CAPITALS across the title page immediately beneath the titles without degrees or designations. Initials should precede the surname. One forename may be given in full according to the author's preference. If there is more than one author the word 'AND' should be placed before the name of the last author.

A line should be typed across the title page below the author(s) name(s) in capitals.

The author(s) name(s) degrees and designations should be typed in lower case below the line. Initials and/or forename should precede the name of each author and his degrees, without full stops between letters, and appointment (e.g. Consultant, Registrar, etc.) should follow it.

A full postal institutional address should follow the names, degrees and appointments. Correspondence will normally be addressed to the first author but, if it is desired to direct correspondence other than to the first author, or if different authors belong to different institutions or departments, a separate sentence should be added: this should start on a new line and begin 'Correspondence should be addressed to . . .' and a full postal address should follow.

SUMMARY AND KEY WORDS

Start a new sheet

The second page should carry a summary of not more than 150 words. The summary should state the purpose of the study or investigation, basic procedures, main findings and their statistical significance, and the principal conclusions.

Do not use abbreviations except for units of measurement (e.g. mg, cm, etc.).

Key (indexing) words. Below the abstract, provide and identify as such, three to 10 key words or short phrases that will assist indexers. Use terms from the Medical Subject Headings list from *Index Medicus*. The Editor may modify these at proof stage to conform with agreed practice of certain other anaesthetic journals in the English language.

COPYRIGHT OFFPRINTS

Authors submitting a manuscript do so on the understanding that if it is accepted for publication, exclusive copyright in the paper shall be assigned to the Association. In consideration for the assignment of copyright, the Publisher will supply 25 offprints of each paper. Further offprints may be ordered at extra cost; the copyright assignment form and the offprint order form will be sent with the proofs. The Association will not put any limitation on the personal freedom of the author to use material contained in the paper in other works.

(continued overleaf)

THE TEXT

Start a new sheet

The text of observational and experimental articles, case reports, etc. is usually divided into sections with the headings *Introduction, Methods, Results* and *Discussion.* Long articles will need subheadings within some sections to clarify their content.

Letters for the correspondence pages should be double spaced and prepared in accordance with the format in a recent copy of *Anaesthesia.*

Headings: three steps of heading may be used in typescripts:

(i) CAPITALS across the centre of the page.
(ii) Underlined words
These should be typed at the left hand side of the page above the paragraph which they precede.
(iii) Underlined words at the beginning of a paragraph. These may either be followed by a full stop or form part of the first sentence of the paragraph.

ACKNOWLEDGMENTS

Start a new sheet

Acknowledge those who have made substantive contributions to the study or the preparation of the manuscript. Authors are responsible for obtaining written permission for publication of reproduced figures and tables from authors and publishers and from everyone acknowledged by name because of copyright conventions and because readers may infer their endorsement of the data and conclusions.

REFERENCES

Start a new sheet

Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by arabic numerals. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. Use double or treble space typing.

Use the form of reference adopted by the U S. National Library of Medicine and used in *Index Medicus.* Use the style of the examples cited at the end of this section.

The titles of journals should be given in full.

Avoid using abstracts as references except those published in a recognised journal. 'Unpublished observations' and 'personal communications' may not be used as references, although references to written, not verbal, communications may be inserted (in parentheses) in the text. Include among the references manuscripts accepted but not yet published; designate the journal followed by (*in press*) in parentheses. Information from manuscript submitted but not yet accepted should be cited in the text as (unpublished observations) in parentheses.

The references must be verified by the author(s) against the original documents.

Examples of correct form of references
Note: first and last pages in all references.

JOURNAL

Standard journal article—(List all authors)
SOTER NA, WASSERMAN SI, AUSTEN KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294:** 687–90.

Corporate author
The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.
Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)
OSLER AG. *Complement: mechanisms and functions.* New York: Prentice-Hall, 1976.

Corporate authors
American Medical Association Department of Drugs. AMA drug evaluations. 3rd ed. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author
RHODES AJ, VAN ROOVEN CE, *comps. Textbook of virology; for students and practitioners of medicine and other health sciences.* 5th ed. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book
WEINSTEIN L, SWARTZ MN Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease.* Philadelphia: WB Saunders, 1974: 457–72.

Agency publication
National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, Md: National Center for Health Statistics, 1972. (*Vital and health statistics. Series* **10:** Data drom the National Health Survey, No. 69) [DHEW publication No. (HSM) 72–1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

ROUECHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

TABLES

Do not include tables in the text. Start a new sheet for each table and space the material adequately. The author(s) name(s) should appear in the top right-hand corner.

Indicate the approximate position of each table in relation to the subject matter of the text in the right-hand margin of the appropriate page on the manuscript. Do not submit tables as photographs. Number tables consecutively with arabic numerals. Supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes. Explain in footnotes all non-standard abbreviations that are used in each table. For footnotes, use the following symbols in this sequence: *, †, ‡, §, ||, ¶, **, ††, etc. Identify statistical measures of variations such as SD and SEM. *Legends for tables* should appear on the face of the table.

Cite each table in the text in consecutive order and mark the approximate position of the table in the right-hand margin of the text.

FIGURES

Each figure should be separate. Do not include figures in the text but collect together in an envelope or folder.

Indicate the approximate position of each figure in relation to the subject matter of the text in the right-hand margin of the appropriate page of the manuscript. Drawings, charts and diagrams should be submitted in black indian ink on a smooth white card and should be about twice the size of that desired in the published version with no lettering. Full plate, glossy black and white photographs will be accepted if they are sufficiently clear. All letters and numerals required on the face of figures must be clearly typed or written on tracing paper firmly attached with self-adhesive tape to the back of the figure and folded over from the front as a cover. They will then be printed in the style of *Anaesthesia* in the exact location indicated. Identify each figure by its sequential number in pencil on the reverse of the illustration and include the title of the paper and the authors' names. Mark the top of the illustration on the reverse by an arrow and the word 'Top'.

All sources of identification of patients must be removed.

LEGENDS FOR FIGURES

Start a new sheet

Type legends for illustrations double spaced with arabic numerals corresponding to the illustrations. When symbols, arrows, numbers or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

CONVENTIONS AND ABBREVIATIONS

Statistics and measurements should be given in figures except that numerals one to nine should be in words if not followed by a measurement symbol (e.g. 'two patients' but '2.0 mg'). The *Système International* (SI) will usually be used except that vascular pressures will be recorded in mmHg and cmH_2O. Imperial measurements will not be used except in an historic context. The 24 hour clock will be used.

Contributors are advised to study the SI *Conversion Tables* provided in the January 1978 issue of *Anaesthesia*, *Units, Symbols and Abbreviations* (*A Guide for Biological and Medical Editors and Authors*) published by the Royal Society of Medicine, London W1M 8AE, and *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1**: 532–5).

LETTERS FOR PUBLICATION

Should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University of Wales Hospital, Heath Park, Cardiff CF4 4XW, UK.

Letters should be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters above. The degrees and diplomas of each author must be given in a covering letter which must be signed personally by all the authors.

Correspondence presented in any other style or format may be the subject to considerable delay and may be returned to the author for revision.

The editors regret that failure to comply with the above requirements may result in a delay in publication of accepted papers.

REVIEW JOURNALS

This journal is covered by *Current Contents*, *ASCA* and the *Science Citation Index*.

Contents: Anaesthesia, vol. 41, no. 1, January 1986

EDITORIAL

Transdermal hyoscine (scopolamine) and postoperative vomiting
J.K. Aronson and J.W. Sear 1

ORIGINAL ARTICLES

Thiopentone levels during cardiopulmonary bypass. Changes in plasma protein binding during continuous infusion
D.J. Morgan, D.P. Crankshaw, P.R. Prideaux, H.N.J. Chan and M.D. Boyd 4
C-reactive protein in patients undergoing cardiac surgery
H. Boralessa, F.C. De Beer, A. Manchie, J.G. Whitwam and B. Pepys 11
Transdermal hyoscine and postoperative nausea and vomiting
J. Uppington, J. Dunnet and C.E. Blogg 16
Intramuscular midazolam premedication in small children. A comparison with papaveretum and hyoscine
M.B. Taylor, P.R. Vine and D.J. Hatch 21
Lower limb blocks for children. Lateral cutaneous and femoral nerve blocks for postoperative pain relief in paediatric practice
L.R. McNicol 27
Longterm treatment with epidural opioids. A retrospective study comprising 150 patients treated with morphine chloride and buprenorphine
P. Carl, M.E. Crawford, O. Ravlo and V. Bach 32
Computerised tomography guided lumbar sympathectomy
D.R.O. Redman, P. N. Robinson and M.A. Al-Kutoubi 39

HISTORICAL

Alfred Kirstein. Pioneer of direct laryngoscopy
N.P. Hirsch, G.B. Smith and P.O. Hirsch 42
Stanley Rowbotham. Twentieth century pioneer anaesthetist
H.A. Condon and E. Gilchrist 46

CASE REPORTS

Phenelzine poisoning
F.X. Breheny, G.J. Dobb and G.M. Clarke 53
Acute upper airway obstruction. Spontaneous retropharyngeal haematoma in a patient with polycythaemia rubra vera
J.W. Mackenzie and J.A. Jellicoe 57
Detection of neurological damage during cardiopulmonary bypass
S.N.C. Bolsin 61
Neonatal tracheal perforation. A complication of tracheal intubation
B.J. McLeod and E. Sumner 67

APPARATUS

Remote monitoring using an induction loop
M.J. Harrison and E.J. Slater 71

FORUM

Cryoanalgesia for pain after herniorrhaphy
R.C. Khiroya, H.T. Davenport and J.G. Jones 73
Epidural buprenorphine for postoperative analgesia. A controlled comparison with epidural morphine
J. Wolff, P. Carl and M.E. Crawford 77

CORRESPONDENCE 80

AUDIOVISUAL REVIEWS 94

ANAESTHETIC LITERATURE 97

NEWS AND NOTICES 106

ANNUAL REPORT OF COUNCIL 120

STOP PRESS 128

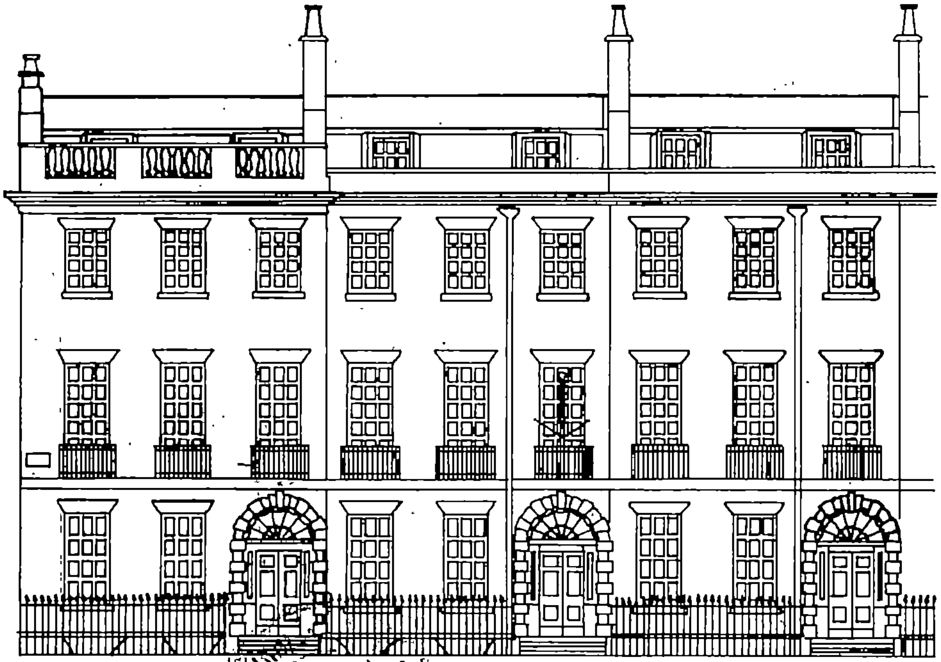
Printed in Great Britain by Fletcher & Son Ltd, Norwich

Acc.
25.9.87

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain & Ireland

Volume 41 Number 2 February 1986



LIBRARY

Published for
The Association of Anaesthetists of Great Britain and Ireland by
Academic Press Grune & Stratton
London Orlando San Diego New York Toronto
Montreal Sydney Tokyo

ISSN 0003-2409

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

Editorial Board
Editor J. N. LUNN
Assistant Editors M. MORGAN, C. E. BLOGG, R. GREENBAUM, R. M. JONES
Chairman P. J. HELLIWELL
Advisory Editors R. S. ATKINSON, T. B. BOULTON
Members C. F. SCURR, P. J. F. BASKETT, D. J. HATCH and a representative of the Junior Anaesthetists Group
Ex officio
The President of the Association T. B. BOULTON
The Honorary Treasurer of the Association M. M. BURROWS
The Honorary Secretary of the Association M.T. INMAN
The Assistant Honorary Secretary of the Association P. MORRIS

Editor Emeritus C. LANGTON HEWER

Sub-editors of special sections
L. KAUFMAN Anaesthetic literature
A. PADFIELD National and local events
G. D. PARBROOK Audiovisual reviews
M. J. HARRISON Computer programs
JACQUELINE WELCH, DIANE WINTERBURN Reference librarians
D. V. BATEMAN Honorary proof reader

Address for literary contributions Dr J. N. Lunn, The Editor, *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK [telephone Cardiff (0222) 763601; Ansafone available].

Neither the Editor nor the Association of Anaesthetists of Great Britain and Ireland is in any way responsible for the statements made or the views expressed by contributors.
Investigations performed on man must conform to appropriate ethical standards including voluntary consent and acceptance by an ethical committee.

Published monthly (January–December) at 24–28 Oval Road, London NW1 7DX, England by Academic Press Inc. (London) Limited for the Association of Anaesthetists of Great Britain and Ireland, Rooms 475–478, Tavistock House South, Tavistock Square, London WC1H 9LG. As from December 2nd 1985, 9 Bedford Square, London WC1B 3RA.

1986, Volume 41, 12 issues. Inland £80.00 inclusive of postage and packing; abroad, $189.00 inclusive of postage and packing. Subscription orders should be sent to Academic Press Inc. (London) Limited, High Street, Foots Cray, Sidcup, Kent DA14 5HP (Tel. 01-300-0155). Send notices of change of address to the office of the Publishers at least 6–8 weeks in advance. Please include both old and new addresses.

Application to pay at second class postage rates pending at Jamaica, New York 11431, U.S.A.

Air freight and mailing in the U.S.A. by Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, U.S.A.

© 1986 The Association of Anaesthetists of Great Britain and Ireland. The appearance of the code at the bottom of the first page of a paper in this journal indicates the copyright owner's consent that copies of the paper may be made for personal or internal use, or for the personal or internal use of specific clients in the U.S.A. This consent is given on the condition, within the U.S.A., that the copier pay the stated per-copy fee through the Copyright Clearance Center Inc., 27 Congress Street, Salem, MA 01970, U.S.A. for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, for resale or for copying or distributing copies outside the U.S.A.

ISSN 0003-2409

Anaesthesia, 1986, Volume 41, pages 129–130

Editorial

A matter of vigilance

There is little doubt that anaesthetic techniques have changed and considerably improved during the last decade, but has the quality of care kept pace with these improvements?

In the investigation into mortality associated with anaesthesia in England, Wales and Scotland, it was shown that there was a mortality directly attributable to anaesthesia of approximately 1 in every 10 000 patients undergoing surgery.[1] More than half these deaths were deemed to have been avoidable. We should ask ourselves, do these avoidable mishaps represent the best that can be achieved in a profession in which the consequence of error is often a major catastrophe, or is there room for improvement? Most, but not all, of these deaths were attributable to human error.

In a recent survey of 150 anaesthetic mishaps which led to claims for damages against anaesthetists who are members of the Medical Protection Society, there is firm evidence that a considerable reduction in the incidence of avoidable mortality and severe morbidity could be achieved by the simple expedient of increased vigilance by individual anaesthetists. Fatigue occasionally seems to be a factor in causing morbidity and mortality due to anaesthesia, particularly when a junior anaesthetist, who has been on duty all night, is expected to work the next day. Unfortunately, a plea of fatigue is no defence in British law, but it may provide mitigating circumstances for the anaesthetist and enable some liability to be placed on the Hospital Authority, should a litigious incident occur. Generally speaking, however, an anaesthetist who accepts the responsibility of care must consider himself fully capable of exercising that duty to the highest standard commensurate with his training. If he is not satisfied with his own ability, it is his responsibility to say so and to arrange for a replacement.

Secondly there is a failure to appreciate the importance of minute-to-minute observations of the 'whole' patient. In four of the 150 cases (3%) in which major damage to the patient occurred as a result of anaesthesia, the patient was known to have been left unattended by the anaesthetist when the crisis occurred. In all these cases, the tragedy could have been avoided if constant vigilance had been exercised. It is certainly not acceptable for a physician anaesthetist working on his own to leave an anaesthetised patient without supervision in the operating theatre during the course of an operation in order to answer the telephone, or for some other reason, even for a short period. If, coincident with his absence the patient dies, or is seriously damaged, the possibility arises that it may demonstrate such reckless and irresponsible behaviour as to attract a charge of manslaughter. An anaesthetist engaged in administering an anaesthetic on his own should never be directly responsible for organising anaesthetic services elsewhere in the hospital, and yet, in the United Kingdom, this practice is not uncommon.

Is there ever any justification for leaving a nurse or paramedical assistant in sole charge of a patient who is being anaesthetised while the physician anaesthetist attends to some problem outside the operating room? In the United Kingdom, where assistants are not usually trained to the standard of the American or Scandinavian nurse anaesthetist, the answer must normally be 'no', and there is little doubt that the courts would take this view unless the anaesthetist could prove convincingly that his absence from the operating room was necessary to save another life, or that the person who remained was sufficiently experienced and trained to undertake the responsibility of supervising a patient under anaesthesia. It should be emphasised that a trainee physician anaesthetist is not really in a different position from a nurse or paramedical assistant merely because he has a medical qualification, unless he has received sufficient postgraduate instruction to make him competent to fulfil the role of deputy.

The relaxation of constant and continuing vigilance also plays a significant part in producing patient morbidity and mortality in the recovery room. Approximately 20% of all cases of death and serious neurological damage related to anaesthesia have occurred during the immediate recovery period. The majority of these tragedies would have been avoided if continuous skilled observations had been made

0003–2409/86/020129 + 02 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

and correctly interpreted. The courts at the present time are likely, in the United Kingdom, to take the view that the anaesthetist is responsible for the well being of his patient until that patient is conscious and his vital functions are stable and can be preserved without assistance. Despite this general understanding, a significant number of anaesthetic-related tragedies have taken place in the recovery room after the anaesthetist had left the operating suite or was otherwise unable to respond to an emergency call. In a number of these cases, the patient had been handed over to the recovery staff (and had been accepted by them) whilst still in a state of profound respiratory depression. This sequence of events will continue to happen in busy hospitals until such time as all anaesthetists and all surgeons recognise the dangers and appreciate that patient safety is much more important than a rapid turnover of surgical cases. The sooner this fact is appreciated the better.

The Medical Protection Society,
50 Hallam Street,
London W.1.

R.A. GREEN

Reference

1. LUNN JN, MUSHIN WW. *Mortality associated with anaesthesia.* Nuffield Provincial Hospitals Trust, 1982.

Editor notices

The Editor and his assistants are grateful to many informal advisors and to the following who have provided formal assessments of manuscripts over the past year.

R. Armstrong
M. Branthwaite
K. Budd
G. Bush
A.J. Byrne
S. Cobbe
Professor C.M. Conway
J. Curran
O.P. Dinnick
J.R. Dodge
P. Gishen
E.R. Grundy
C.E.W. Hahn
G.M. Hall
D.J. Hatch
B. Hayes
J.G. Jones
L. Kaufman
J.H. Kerr
H. McQuay
Professor W.W. Mapleson
P. Morris
Professor J. Norman
J.F. Nunn
Professor C. Prys-Roberts
J.W. Sear
M. Stark
Professor M. Sussman
F.J. Walters
S.M. Willatts
J. Watkins

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Univorm requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

News and Notices sections

The first issue of each quarter will contain full News and Notices sections.

Copy dates for these will be: 14 March 1986 for June 1986, 13 June 1986 for September 1986 and September 1986 for January 1987.

Supplementary News and Notices sections will be published in other issues but they will contain only material which requires publication before the next full News and Notices section.

Anaesthesia, 1986, Volume 41, pages 131–137

Nuclear magnetic resonance

Its implications for the anaesthetist

C. NIXON, N. P. HIRSCH, I. E. C. ORMEROD AND G. JOHNSON

Summary

The theory and practice of clinical nuclear magnetic resonance (NMR) imaging is reviewed. Problems which the anaesthetist will encounter are considered, and recommendations are proposed. Possible uses of NMR in anaesthesia are discussed.

Key words
Measurement techniques; nuclear magnetic resonance.

The last decade has witnessed a revolution in non-invasive techniques for imaging anatomical structures. The use of ultrasound is now widespread, and computerised tomographic scanning (CT) is well established in many centres throughout the world. The American development of positron emission tomography (PET), permits imaging of body structures by 'visualising' certain biochemical events, such as oxygen uptake. The latest imaging innovation in clinical medicine is that of nuclear magnetic resonance (NMR). The origins of this technique stem from the post war work carried out independently by Purcell *et al.*,[1] and Bloch *et al.*,[2] who jointly received a Nobel prize in 1952 for their discovery of the phenomenon of NMR. Within a few years it was discovered that the resonant frequency of nuclei of the same element is dependent on their environment. This became known as the 'chemical shift',[3] and led to the development of NMR spectroscopy. However it was Lauterbur,[4] 21 years later, who suggested that the technique could be used for imaging. NMR imaging was developed by several groups over the next few years and clinical trials were begun in the 1980s.

With the expansion of the clinical application of imaging, the problems of safely examining patients with impaired conscious level, whether from illness, sedation or general anaesthesia, have to be approached. A recent report[5] has demonstrated that the resolution of the NMR image is improved when the ventilation is controlled rather than spontaneous, but as yet there is little published on this subject. This paper sets out to inform the anaesthetist of the difficulties that will be experienced in providing anaesthesia for NMR imaging, and looks at the potential use of NMR in future anaesthetic research.

C. Nixon, MB, ChB, FFARCS, Senior Registrar in Anaesthetics, N.P. Hirsch,* MB, BS, FFARCS, Senior Registrar in Anaesthetics, I.E.C. Ormerod, MB, BS, MRCP, NMR Research Fellow, Honorary Registrar in Neurology, G. Johnson, PhD, M.Inst.P, NMR Research Fellow (Physics), The Institute of Neurology and The National Hospital for Nervous Diseases, Queen Square, London WC1.

Correspondence should be addressed to: Dr C. Nixon, The Hospital for Sick Children, 555, University Avenue, Toronto, Ontario, M5G 1X8 Canada.

*Currently Instructor in Anesthesiology, Yale University, New Haven, Connecticut, U.S.A.

0003–2409/86/020131 + 07 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Theory

NMR and NMR imaging have been extensively reviewed in the literature.[6-8] Atomic nuclei with an odd number of protons and/or neutrons (e.g. ^1H, ^{31}P, ^{13}C) have intrinsic magnetic properties, and behave like minute bar magnets. When a sample containing such nuclei is placed in a large magnetic field, the nuclei tend to align and rotate or 'process' to lie parallel with the field. The result is a net nuclear magnetisation in the axis of the applied magnetic field. The precession occurs at a specific frequency w_o, which is dependent on the gyromagnetic properties of the nuclei involved γ, and is directly proportional to the strength of the magnetic field B_o, measured in Tesla (T). This precession frequency w_o is given by the Larmor equation:

$$w_o = \gamma\ B_o$$

For imaging, we are mainly concerned with hydrogen nuclei, a single proton, for which $\gamma = 42.6\ \mathrm{MHz\ T^{-1}}$ and w_o is in the radiofrequency range of the electromagnetic spectrum. A pulse of radiofrequency (RF) energy directed into the sample at or near the Larmor frequency, will knock the nuclei out of alignment. By varying the duration of the RF pulse, the degree of rotation varies, typically to 90 or 180 degrees. Once the pulse is removed, the nuclei rotate back to their original position in an exponential way. As this occurs, they emit an RF signal at the same Larmor frequency. Two time constants describe the RF signal decay, T_1 and T_2. T_1 is the longitudinal relaxation time, and describes the time for the vector of the spins to revert to their original orientation along the magnetic field. Relaxation in the transverse direction is termed the spin–spin relaxation, characterised by the time constant T_2. T_1 is dependent on the interaction of protons with surrounding nuclei and molecules (the lattice), while transverse relaxation (T_2) depends on the interaction of identical protons with each other.

In an imaging experiment, the patient is placed in a large homogeneous magnetic field, typically with a strength of about 0.5 Tesla. This corresponds to a proton resonant frequency of about 21 MHz. The protons are excited by a radiofrequency pulse at the Larmor frequency. The strength of this pulse is about 15 μT. The patient is then subjected to gradient magnetic fields which cause protons in different positions to precess at different frequencies. The gradients are usually about 5 mT/m and are switched on and off in about 1 m second. The precessing spins induce a voltage of tens of μV in the receiver coil. Signals are collected with a number of different combinations of magnetic field gradients and projections to enable the image to be reconstructed by computer, using two dimensional Fourier transformation.[9]

Hazards of NMR to the patient

The advantage claimed for NMR imaging over scanning methods utilising ionising radiation is improved patient safety.[10] However, three distinct sources of potential hazard to the patient exist. These are the static magnetic field, the changing magnetic field gradients and the RF field.

Static magnetic fields. These are believed to be safe,[11] even with prolonged exposure. The present generation of NMR imagers use a static field in the range of 0.1–2 T. No adverse effects have been associated with static fields up to 2 T, and the US Bureau of Radiological Health[12] suggests this level should not be exceeded. However, the static magnetic field may prove hazardous in certain patients with implanted ferromagnetic devices. New *et al.*,[13] have reported that the magnetic field during NMR imaging is sufficient to produce dislocation of certain vascular clips from blood vessels. For this reason, manufacturers are adopting nickel and titanium alloys for clips. It has also been reported[14] that certain cardiac pacemakers are switched from demand to fixed rate pacing when in the vicinity of a large static NMR field magnet. In addition, pacemakers with ferromagnetic casings may be rotated or displaced within the chest wall. Static magnetic fields exceeding 0.3 T cause T-wave abnormalities of the electrocardiogram.[15,16] These changes increase linearly with field strengths up to 2 Tesla, and are thought to be due to induced EMF associated with blood flow perpendicular to the magnetic field. These T-wave changes revert to normal when the magnetic field is removed and are not associated with dysrythmias, changes in blood pressure or heart rate.[17]

The high static magnetic field may propel loose ferromagnetic material e.g. metal badges, safety pins or scissors around the room and may be hazardous to the patient or staff. Anaesthetic equipment will also be attracted by the field, items should therefore be permanently mounted if placed near to the imager. Analogue wrist watches may be damaged, and magnetic data may be erased from credit cards and magnetic storage material (cassette tapes, floppy discs, etc).

Changing magnetic fields. The rapidly changing magnetic fields that are superimposed on the main static field generate internal electrical currents (induced EMF's). The current density induced during clinical NMR imaging is of the magnitude of 10 mA/sq m. A current density of 170 mA/sq m is required to induce visual light flash sensations (magnetic phosphenes), 1–10 A/sq m induces heart fibrillation and 30 A/sq m induces a nerve action potential. Although the EMF induced by NMR is low, patients with cardiac pacemakers may be at risk. The voltage induced in the pacemaker lead is insufficient to be registered as normal cardiac activity, but the microcircuitry may be affected, resulting in failure of normal output.[14] A theoretical hazard also exists for patients with epilepsy,[18] where rapid repetition of changing magnetic field gradients may induce seizures. To date, there have been no clinical reports of this complication.

Radiofrequency effects. There is already extensive literature[19,20] concerning human exposure to RF radiation. Heat production at the power levels currently employed in NMR imaging is unlikely to cause adverse effects. Problems may be encountered with patients with metallic implants where local heating can occur. *In vitro* testing of surgical clips and hip prostheses demonstrated small temperature rises with RF signal strengths much greater than those used in clinical NMR imaging. The authors recommended that individuals with large metallic implants should not be imaged until further investigations are completed to evaluate the RF heating effects more thoroughly.[21]

Other problems unrelated to magnetism are also worthy of mention, notably those of claustrophobia and noise. The Picker imager at the National Hospital, Queen Square has internal dimensions of 2 metres length × 0.6 metre diameter. It is therefore not surprising that claustrophobia occurs, particularly as the average scan time is 40 minutes. Other groups have reported the incidence of claustrophobia to be 3–4%,[22] but in our unit the incidence is around 7%. During imaging, a drumming noise is emitted which some patients find unpleasant. In our unit, three patients have succeeded in escaping from the imager and the less cooperative patient may therefore require sedation prior to imaging.

Anaesthesia for NMR imaging

In addition to the hazards discussed above, the anaesthetist will encounter other problems. These can be divided into two main categories, anaesthetic equipment and monitoring.

Anaesthetic equipment

The magnetic effects of NMR imaging impose various restrictions on the anaesthetic equipment used. Within the bore of the magnet, all ferromagnetic components should be avoided. The imaging process is very sensitive to magnetic field inhomogeneities and even mildly ferromagnetic objects can distort the field sufficiently to degrade the image (Figs, 1a and b). Large non-ferromagnetic metal objects may also have a detrimental effect on the RF excitation pulses and the reception of the NMR signal. Outside the bore of the magnet, large ferromagnetic objects may cause image distortion and both large and small objects can be drawn into the magnet.

Most metallic equipment is constructed of alloys which vary in their ferrous content and therefore the attractive force in a magnetic field. We have tested a number of items at the portal of our 0.5 T imager, using the method of New *et al.*[13] Anaesthetic equipment was suspended in the magnetic field, the angle of deflection from the vertical on the long (z) axis of the imager being related to the magnetic force of attraction (F) by the formula $F = mg\tan\theta$ where m is the mass of the object, g the gravitational acceleration and θ the angle of deflection. The results are shown in Table 1. The safest approach is to avoid all metallic equipment and substitute apparatus of plastic or nylon manufacture wherever possible. Non-ferromagnetic alternatives are available for commonly used anaesthetic equipment, but there is a problem when considering laryngoscopes. Table 1 shows it is the batteries within the laryngoscopes which are highly ferromagnetic, making them unwieldy in close proximity to the NMR imager. Hospital trolleys have been used to transfer patients to our imager, but they must be removed during imaging as they

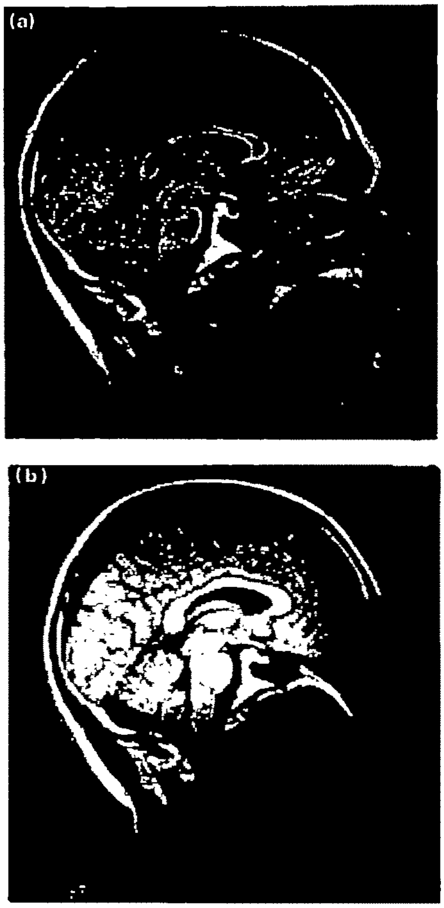


Fig. 1. (a) NMR image of the head and neck demonstrating the excellent image quality. (b) Similar view of the same patient demonstrating loss of image quality due to a metallic tracheal tube connector.

can degrade the signals. Certain NMR imagers (e.g. General Electric) now feature a detachable patient table which allows preparation of the patient distant from the imager.

There is considerable danger associated with large ferromagnetic objects for which no alternatives can be found (e.g. gas cylinders). Unlike the inverse square that applies to ionising radiation, the magnetic field strength B, at a point P on the z axis of a solenoid or toroid approximates to the formula; $B = 1 - \cos\theta$ (Appendix 1). Consequently, the force acting on large ferromagnetic objects introduced into the magnetic field increases so rapidly as the imager is approached (Fig. 2), that it may be impossible to restrain them. We feel that in the interests of safety, large ferromagnetic objects should only be taken within the 0.5 mT zone with extreme caution. The extent of this zone is dependent on the magnetic field strength and shielding of the imager in use, and is approximately 3 metres from the portal of our 0.5 T magnet. As field strength falls off more rapidly to the sides of the magnet than

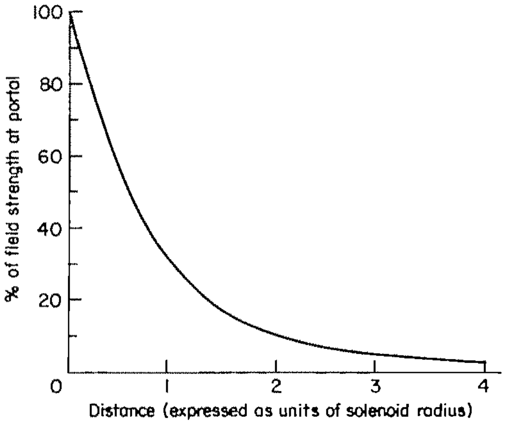


Fig. 2. Relationship of magnetic field strength to distance from the solenoid portal.

Table 1. Magnetic force on anaesthetic apparatus at NMR portal

	Weight (g)	Angle of deflection	Force (newtons)	Recommended apparatus
Laryngoscope	253	55	3.54	No satisfactory substitute
Batteries removed	170	1	0.029	
Blade	85.3	0	0	
Tracheal tube connectors				
Robotham	19.97	1.5	0.005	Plastic connector 15 mm
Magill	24.28	1	0.004	
Standard tubing connector	26.64	0.5	0.002	Plastic 22 mm connector
90° angle piece	89.1	0.5	0.0076	
Butterfly needle (Abbott)	0.23	3.5	0.0001	Elastomeric cannula
Scissors	31.74	86	4.453	
Ballpoint pen	18.86	10	0.033	

along its *z* axis, this would be the safer position for the anaesthetic machine. The superconducting magnets used in NMR imagers are energised at all times and are kept at an operating temperature of −270K by helium and nitrogen. Static field effects are therefore always present. In emergency situations, this must be borne in mind. Access to the patient in the imager requires cessation of scanning and removal of the patient from the magnet bore.

Anaesthesia in the enclosed environment of any NMR imager requires that the tracheas of all patients are intubated for airway control. Patients undergoing imaging of the head and neck region are placed within a smaller coil to improve signal to noise ratio. In these patients we prefer a Rae pattern oral tube with 15 mm connector as space is inadequate for standard connectors. The choice between spontaneous or controlled ventilation is a matter for the individual anaesthetist, but it is important to consider the choice of breathing system and the ventilator. Two approaches are possible; firstly, the anaesthetic machine is placed remotely, with the ventilator and delivery system sited near to the portal of the imager; secondly, the anaesthetic machine and ventilator are placed remotely. A long breathing system is then required to deliver fresh gas to the patient (typically 5–6 metres, though this will vary with the imager in use).

If the former approach is adopted, the ventilator should ideally be of low mass, have no ferrous components, and its performance should not be influenced by the static field. A fluidic ventilator (Monaghan 225 volume ventilator), placed at the portal of a 0.5 T imager, has been successfully employed in six patients; its performance is unaffected by the static magnetic field.[23]

In addition to the avoidance of metallic connectors, the chosen breathing system should have a low expiratory resistance as this increases with length. Standard 22 mm tubing (ISO 5367:1980) was found to have a resistance of approximately 7 Pa/metre at 30 litres/minute and 15 Pa/metre at 60 litres/minute. The major contributor to resistance is the adjustable pressure limited valve, whose performance has been shown to be variable.[24] Coaxial breathing systems are lighter and more compact and are therefore attractive, but they may suffer from increased expiratory resistance.[25]

Monitoring the patient

A patient placed in the bore of a NMR imager will be hidden from view, and it is therefore necessary to monitor vital functions. Ferromagnetic equipment within the bore of the magnet must be avoided but, in addition, loops of wire (even non-ferromagnetic wire) from monitoring equipment within the bore can significantly degrade RF excitation pulses and NMR signal detection. All direct electrical connexions between equipment within the magnet and outside may introduce RF interference and must be avoided. Fibre-optic systems can be substituted[26] for wires where it is necessary to transfer an electrical signal. The changing gradient fields and the RF pulses may interfere with the operation of monitoring equipment. Careful design is necessary to avoid, filter out or gate out spurious signals induced in monitoring transducers. Cathode ray tubes should be kept away from the magnet to prevent distortion of the display.[27]

Breathing has been monitored using a rubber pneumatic bellows linked to a pressure sensitive piezo-electric crystal outside the magnet room by a pressure line so as not to interfere with data acquisition.[28] We have successfully used apnoea alarm mattresses, and capnography (Engstrom Eliza) to monitor respiratory rate. The gas analyser must be of the remote sampling type, and will require additional length to be added to the fine bore sampling tube. End-tidal CO_2 readings must be interpreted with suspicion.

Blood pressure can be monitored with a non-invasive, automated blood pressure monitor, e.g. utilising an oscillometric method (Dinamap); in such cases, the metallic tubing connectors are replaced by nylon connectors. When continuous arterial line monitoring is required there must either be a long pressure line or pressure signals may be carried by fibre-optics to eliminate the effect of changing magnetic fields.

NMR spectroscopy and anaesthesia

In vivo spectroscopy is a rapidly developing clinical technique, enabling study of biochemical, physiological and pharmacological events. Though the techniques are somewhat different, the basic principles are similar.

^{31}Phosphorus spectroscopy is a non-invasive method of measuring intracellular phosphate levels; this is particularly important in the study of muscle. Intracellular levels of pH, phosphocreatinine, adenosine triphosphate (ATP), and inorganic phosphate can be recorded. Using this technique, bupivacaine has been shown[29] to have a direct myotoxic effect when injected intramuscularly in rats. The diagnosis of muscle disorders without resort to biopsy may be possible. Already, McArdle's syndrome, a rare genetically determined disorder of muscle characterised by intermittent weakness, pain and stiffness, especially after exercise, has been diagnosed in a patient by ^{31}P-NMR.[30] In addition, ^{31}P has also been used to demonstrate changes in cerebral metabolism with regional blood flow.[31] The accuracy of ^{31}PNMR studies of cellular metabolism has been questioned however,[32] as discrepancies do occur between NMR derived metabolic levels and those of classical extraction techniques.

Perhaps of greater interest to anaesthetists is the ability to image ^{19}fluorine. Many synthetic drugs contain fluorine, including volatile anaesthetic agents (e.g. halothane, enflurane, etc), blood substitutes (e.g. perfluorotributylamine), butyrophenones (e.g. haloperidol) and steroids (e.g. dexamethasone). Workers using this technique have demonstrated the distribution of halothane in rabbit brain,[33] the elimination of halothane and isoflurane from rabbit brain[34] and the distribution of halothane and enflurane in the blood of dogs.[35] ^{19}F spectroscopy of CF_4 gas has successfully been used to assess ventilation in excised rabbit lung,[36] whilst phantom limb vasculature has been demonstrated with perfluorotributylamine.[33]

The suggestion that NMR may be useful in monitoring the effectiveness of drug therapy follows work by Davis *et al.*[37] They used NMR to distinguish between sterile and infected abscesses induced in rats, though doubt exists as to the suitability of their animal model. The application of scintigraphy and NMR in pharmacology is well reviewed by Carr.[38]

Conclusions

Although clinical NMR imaging is in its infancy, its future seems assured. As the role of NMR widens, a growing number of patients and anaesthetists will become involved with this technology. It is hoped that not only will NMR imaging provide a service for our patients, but also open new avenues for research within the specialty of anaesthesia.

Acknowledgments

The authors wish to express their gratitude to Dr D. Jewkes, Dr G.S. Ingram, Dr I. Calder, Dr L. Loh and Dr B. Kendall of the Departments of Radiology and Anaesthetics of the National Hospital for Nervous Diseases, Queen Square, London for their help in the preparation of this manuscript.

Appendix 1

Magnetic field strength along the axis of a solenoid is given by the formula

$$B = \frac{u\,n\,I}{2}.\ (\cos\theta_2 - \cos\theta_1)$$

where B = Magnetic field strength (Tesla); u = permeability of medium; n = turns per metre of coil; I = current flowing through the coil (amperes); θ_2 = angle from point P to distant end of coil; θ_1 = angle from point P to nearer end of coil.

If the solenoid is of infinite length, then for a point P lying outside the solenoid $\theta_2 = 0$ degrees, therefore $\cos\theta_2 = 1$. Thus, the formula may be rewritten as

$$B = \frac{u\,n\,I}{2}.\ (1 - \cos\theta_1)$$

References

1. Purcell EM, Torrey HC, Pound RV. Nuclear induction. *Physical Review* 1946; **69:** 37–8.
2. Bloch F, Hansen WW, Packard ME. Resonance absorption by nuclear magnetic moments in a solid. *Physical Review* 1946; **69:** 127.
3. Proctor WG, Yu GC. The dependence of nuclear magnetic resonance frequency upon chemical compound. *Physical Review* 1950; **77:** 717.
4. Lauterbur P. Image formation by induced local interactions: examples employing nuclear magnetic resonance. *Nature* 1973; **242:** 190.
5. Schultz CL, Alfidi RJ, Nelson AD, Kopiwoda SY, Clampitt ME. Effect of motion on two dimensional fourier transformation magnetic resonance images. *Radiology* 1984; **152:** 117–21.
6. Pykett IL, Newhouse JH, Buonanno FS, Brady TJ, Goldman MR, Kistler JP, Pohost GM. Principles of nuclear magnetic resonance imaging. *Radiology* 1982; **143:** 157–68.
7. Partain CL, James AE, Rollo FD, Price RR. *Nuclear magnetic resonance imaging*. Philadelphia: W.B. Saunders, 1983.
8. Young SW. *Nuclear magnetic resonance imaging*,

basic principles. New York: Raven Press, 1984.

9. Edelstein WA, Hutchinson JMS, Johnson G, Redpath T. Spin warp NMR imaging and applications to human whole body imaging. *Physics in Medicine and Biology* 1980; **25**: 751–6.
10. Koeze TH. Applications of nuclear magnetic resonance in medicine. *British Journal of Hospital Medicine* 1982; **27**: 402–7.
11. Budinger TF. Nuclear magnetic resonance (NMR) *in vivo* studies: known thresholds for health effects. *Journal of Computer Assisted Tomography* 1981; **5**: 800–11.
12. Department of Health and Human Services, PHS, FDA. Bureau of Radiological Health, Division of Compliance. Guidelines for evaluating electromagnetic risk for trials of clinical NMR systems, Feb 25, 1982. 1.
13. New PFJ, Rosen BR, Brady TJ, Buonanno FS, Kistler JP, Burt CT, Hinshaw WS, Newhouse JH, Pohost GM, Taveras JM. Potential hazards and artifacts of ferromagnetic and nonferromagnetic surgical and dental materials and devices in nuclear magnetic resonance imaging. *Radiology* 1983; **147**: 139–48.
14. Pavlicek W, Geisinger M, Castle L, Borkowski GP, Meaney TF, Bream BL, Gallagher JH. The effects of nuclear magnetic resonance on patients with cardiac pacemakers. *Radiology* 1983; **147**: 149–53.
15. Gaffey CT, Tenforde TS, Dean EE. Alterations in the electrocardiogram of baboons exposed to DC magnetic fields. *Bioelectromagnetics* 1980; **1**: 209.
16. Togawa T, Okai O, Oshima M. Observation of blood flow E.M.F. in externally applied strong magnetic fields by surface electrodes. *Medical and Biological Engineering* 1967; **5**: 169–70.
17. Tenforde TS, Gaffey CT, Mayer BR, Budinger TF. Cardiovascular alterations in Macaca monkeys exposed to stationary magnetic fields; experimental observations and theoretical analysis. *Bioelectromagnetics* 1983; **4**: 1–9.
18. Hoult DI. Medical imaging by NMR. In: *Magnetic resonance in biology* Volume 1. Cohen JS, ed. New York: John Wiley & Sons, Inc. 1980.
19. Bottomley PA, Andrew ER. RF magnetic field penetration, phase shift and power dissipation in biological tissue: implications for NMR imaging. *Physics in Medicine and Biology* 1978; **23**: 630–43.
20. Bottomley PA, Edelstein WA. Power dissipation in whole body NMR imaging. *Medical Physics* 1981; **8**: 510–2.
21. Davis PL, Crooks L, Arakawa M, McKee R, Kaufman L, Margulis AR. Potential hazards in NMR imaging: heating effects of changing magnetic fields and RF fields on small metallic implants. *American Journal of Roentgenology* 1981; **137**: 857–60.
22. Bydder GM. Clinical nuclear magnetic resonance imaging. *British Journal of Hospital Medicine* 1983; **29**: 348–56.
23. Dunn VD. Magnetic resonance imaging and mechanical ventilation. *Programs of the Society of Magnetic Resonance in Medicine* 1984; 199.
24. Nott MR, Norman J. The resistance of Heidbrink-type expiratory valves. *British Journal of Anaesthesia* 1978; **50**: 477–80.
25. Humphrey D. The Lack, Magill and Bain anaesthetic breathing systems: a direct comparison in spontaneously breathing anaesthetized adults. *Journal of the Royal Society of Medicine* 1982; **75**: 513–24.
26. Rolfe RP. *Fetal and neonatal physiological measurements*. London: Pitman Medical, 1981.
27. Higgins CB, Lanzer P, Stark D, Botvinick E, Schiller NB, Crooks L, Kaufman L, Lipton MJ. Imaging by nuclear magnetic resonance in patients with chronic ischemic heart disease. *Circulation* 1984; **69**: 523–31.
28. Roth JL, Nugent M, Gray JE, Julsrud PR, Berquist TH, Sill JC, Kispert DB. Patient monitoring during magnetic resonance imaging. *Anesthesiology* 1985; **62**: 80–3.
29. Newman RJ, Radda GK. The myotoxicity of bupivacaine, a ^{31}P NMR investigation. *British Journal of Pharmacology* 1983; **79**: 395–9.
30. Ross BD, Radda GK, Rocker G, Esiri M, Falconer-Smith J. Examination of a case of suspected McArdles syndrome by ^{31}P nuclear magnetic resonance. *New England Journal of Medicine* 1981; **304**: 1338–42.
31. Ackermann JJH, Bore PJ, Gadian DG, Grove TH, Radda GK. NMR studies of metabolism in perfused organs. *Philosophical Transactions of the Royal Society of London* 1980; **289**: 425–36.
32. Balaban RS. The application of nuclear magnetic resonance to the study of cellular physiology. *American Journal of Physiology* 1984; **246**: C10–C19.
33. Wyrwicz AM, Pszenny MH, Schofield JC, Tillman PC, Gordon RE, Martin PA. Noninvasive observations of fluorinated anesthetics in rabbit brain by fluorine-19 nuclear magnetic resonance. *Science* 1983; **222**: 429–30.
34. Wyrwicz AM, Ryback K, Pszenny MH, Nichols BG, Tillman PC. *In vivo* ^{19}F NMR study of fluorinated anesthetics elimination from a rabbit brain. *Programs of the Society of Magnetic Resonance in Medicine* 1984; 763–4.
35. Burt CT, Roberts J, Lojeski E, Hitzig B. ^{19}F NMR evaluation of the binding of halothane to erythrocytes, serum and whole blood. *Programs of the Society of Magnetic Resonance in Medicine* 1982; 35–6.
36. Heidelburger E, Lauterbur PC. Gas phase ^{19}F NMR zeugmatography: a new approach to lung ventilation imaging. *Programs of the Society of Magnetic Resonance in Medicine* 1982; 70–71.
37. Davis PL, Crooksle, Kaufman L, Herkens R, Margulis AR. NMR imaging *in vivo* in animals. *Programs of the Society of Magnetic Resonance in Medicine* 1982; 48–9.
38. Carr EA. Scintigraphy and nuclear magnetic resonance: their potential applications in pharmacology: new radiopharmaceuticals and spin drugs: their potential implications for scintigraphy and nuclear magnetic resonance. *Clinical Pharmacology and Therapeutics* 1984; **35**: 131–40.

Anaesthesia, 1986, Volume 41, pages 138–142

In vitro buffering capacity of Alka Seltzer Effervescent

A comparison with magnesium trisilicate mixture B.P. and sodium citrate 0.3 M

G. C. MURRELL AND M. ROSEN

Summary

The variety of antacids used as a prophylaxis for acid aspiration syndrome reflects dissatisfaction with each agent. Alka Seltzer Effervescent is a proprietary product without aspirin. We have shown that it can easily be dissolved in a small volume, readily mixes with hydrous fluids, and has a satisfactory neutralising capacity. Its non-particulate nature, storage in individual packages and palatability, indicated by commercial acceptance overseas, show that further trials in vivo *as a method of raising gastric pH may be useful.*

Key words

Complications; aspiration, prophylaxis.

Antacids are used to raise intragastric pH above 2.5 as a prophylactic for acid aspiration syndrome.[1] However, each agent has some problem. Magnesium trisilicate mixture (MMT) is particulate, which may have been a cause of pneumonitis,[2] mixes poorly with gastric contents so that gastric pH is not uniformly raised, contains peppermint oil which reduces lower oesophageal sphincter pressure and settles concreting in storage.[3] Sodium citrate (0.3M) only has a shelf life of about 8 weeks,[4] which introduces problems with manufacturing. It is not palatable and is slightly more expensive than MMT.

Alka Seltzer Effervescent is a commercial 'over-the-counter' preparation in the United States, where there is a demand for antacids without aspirin. A previous study[5] has shown that intragastric pH before emergency general surgery was satisfactorily increased by use of two tablets dissolved in 20 ml of water. In dogs, no change occurred in oxygenation, intrapulmonary shunting, or pulmonary vascular resistance after instillation of Alka Seltzer solution into the lungs. One tablet of Alka Seltzer Effervescent contains sodium bicarbonate, potassium bicarbonate, and citric acid, which is converted to citrate with loss of carbon dioxide when the tablet is dissolved in water. Thus, the solution mainly contains sodium and potassium citrates.

This study compares the buffering capacity and miscibility of Alka Seltzer Effervescent with magnesium trisilicate mixture (B.P.) and 0.3M sodium citrate.

Method

The pH measurements were made with a Phillips digital pH meter PW 9409, with the slope set between 95 and 100%, after calibration with

---

G.C. Murrell, FFARCSI, Registrar, M. Rosen, FFARCS, Honorary Professor, University Hospital of Wales, Heath Park, Cardiff CF4 4XW.

Correspondence should be addressed to Professor Rosen please.

0003–2409/86/020138 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

universal phosphate buffer pH 7.4 and acid phosphate buffer pH 1.0 before each test period. Initial tests showed that the calibration was satisfactory for at least 20 individual measurements with a standard variation of 0.006 around the pH 7.40 reference. Recalibration was carried out after two titrations.

Titration was carried out with 1M hydrochloric acid added rapidly in 2 ml aliquots from the burette, during continuous stirring of the mixture. This acid solution is ten times stronger than normal gastric acid, but the volumes were more convenient and it provided a severe test of buffering capacity for each antacid.

The effect of timed exposure to air

Two Alka Seltzer tablets dissolved in 20 ml of water, 30 ml of 0.3M sodium citrate and 20 ml of MMT were tested for buffering capacity at intervals of 0, 2, 5, 10, 15 and 30 minutes after exposure to air, to determine loss of potency by carbon dioxide emission. At 1 minute, Alka Seltzer tablets were still effervescent, so 2 minutes was used as the starting point.

The buffering capacity of antacid solutions

The buffering capacities of the 20 ml solutions of Alka Seltzer containing 1, 2, 3 or 5 tablets, 30 ml of 0.3M sodium citrate and MMT 20ml were tested by titration. In a non-particulate mixture, the new pH was reached within seconds, but MMT was much less consistent as, even with stirring, the pH reading 'wandered'. However, if it had not settled by 3 minutes, the reading was recorded and the titration proceeded.

Mixing of antacid solutions

The ability of an antacid solution to mix with an acid was tested by slowly adding the antacid to the surface of 100 ml of 0.1M hydrochloric acid (pH 1) via a narrow stemmed funnel. Addition was completed in 60 seconds. The mixture was not stirred initially and the pH measured at two marked levels (by gently raising and lowering the pH electrode) at 5-minute intervals for 30 minutes. The upper level was set with the electrode just sufficiently covered for consistent readings, as shown by a prior test with buffer. The lower level was just above a point at which a prior test showed an interface. After 30 minutes the mixture was stirred, once initially, then if no change occurred after 5 minutes, one stir was applied again and if still little or no change occurred, the mixture was stirred vigorously.

Results

Alka Seltzer acted as a buffer, preventing change in pH as acid is added, much more effectively than the same volume of water (Fig. 1). The vertical line on this figure and all other figures, corresponds to the volume of acid containing the same number of hydrogren ions as would be found in 100 ml of gastric juice at pH1. The intercept of this line allows a comparison between antacids of their efficacy in raising the pH of gastric juice. As a buffer curve intercepts at a pH of 5.3 it is reasonable to expect it to raise the gastric pH to above the safety margin of 2.5–3.5 after ingestion.

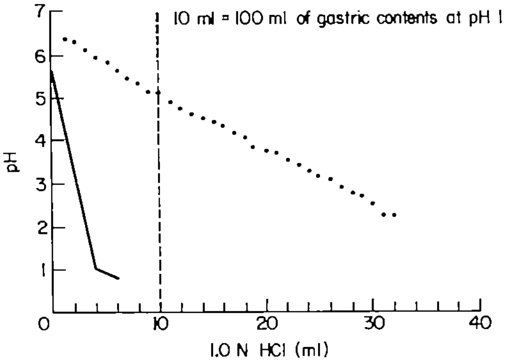


Fig. 1. Comparison of pH change on adding acid to 20 ml of water or Alka Seltzer solution. The dotted line illustrates the usual maximum hydrogen ion load found in the gastric contents. (———), water; (....), Alka Seltzer.

Effect of exposure to air

Figures 2 and 3 show that standing open to atmosphere has little effect on the buffering capacity of 0.3M sodium citrate or Alka Seltzer in the short term. MMT showed no consistent change with time, and the differences in Fig. 4 are probably due to inadequate mixing.

Buffering by different solutions

The buffering capacity of one tablet of Alka Seltzer is markedly less than that of two tablets, but even so one tablet is still able to raise the pH

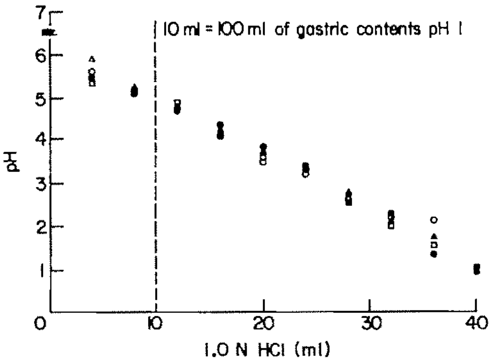


Fig. 2. Buffering capacity of Alka Seltzer after exposure to air when initial effervescence has ceased. Two tablets in 20 ml, titration commencing at (●), 2 minutes; (▲). 5 minutes; (□), 15 minutes; (○), 30 minutes.

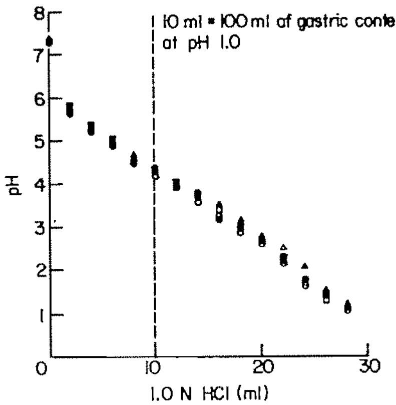


Fig. 3. Buffering capacity of 20 ml sodium citrate 0.3M after exposure to air. Titration commencing at (●), 2 minutes; (○), 5 minutes; (△), 15 minutes; (□), 30 minutes.

of the equivalent of 100 ml of gastric fluid to above 3.5 (Fig. 5). It can also be seen from this figure that three and five tablets are little better than two tablets. There is a small amount of precipitate after dissolving two tablets, but this is more obvious after five are dissolved in 20 ml. This precipitate completely disappears after addition of a few millimetres of acid. Thus, there are not likely to be any particles after mixing with gastric contents.

Comparison of antacids by means of titration revealed them all as satisfactory. Sodium citrate 0.3M had the lowest intercept, with a line representing the hydrogen ion content of 100 ml of gastric juice, Alka Seltzer seems slightly better, and MMT, despite wider variation, was able to maintain a high pH in the face of an acid challenge.

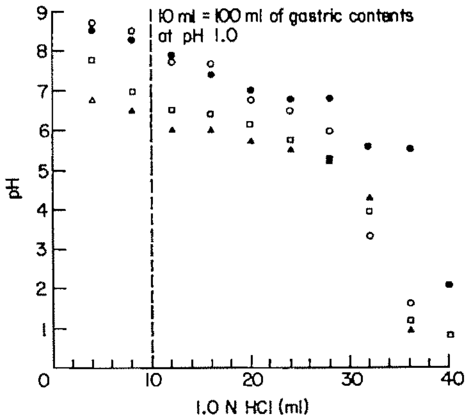


Fig. 4. Buffering capacity of magnesium trisilicate mixture B.P. after exposure to air and with agitation during titration. Titrations commencing at (●), 2 minutes; (△), 5 minutes; (□), 15 minutes; (○), 30 minutes.

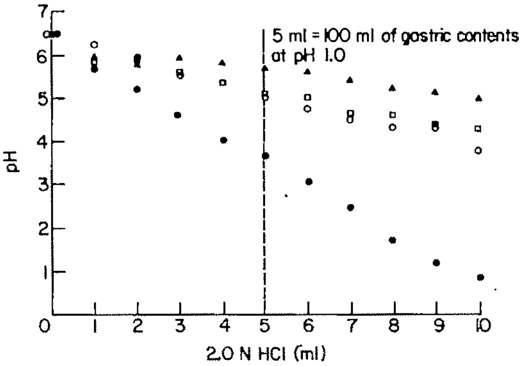


Fig. 5. Buffering capacity of different numbers of Alka Seltzer tablets dissolved in 20 ml of water with titration commenced at 2 minutes. (●), 1 tablet; (○), 2 tablets; (□), 3 tablets; (△), 5 tablets.

Mixing with acids

Table 1 shows that it was easy to make a separate layer with each antacid. MMT initially sat on the surface of the acid but, as the full amount was added, sank as a mass, leaving an oily appearance on the surface. Sodium citrate and Alka Seltzer slightly raised the pH of the solution close to the interface even without agitation, Alka Seltzer slightly more so. After the second stir, Alka Seltzer had raised the pH slightly more than

Table 1. Change of pH in acid–antacid mixture with an without stirring

	Magnesium trisilicate		0.3 sodium citrate		20 ml solution of 2 tablets of Alka Seltzer	
	pH at		pH at		pH at	
Time of measurement	Upper level	Lower level	Lower level	Upper level	Lower level	Upper level
Before addition of antacid	1.05	—	0.98	—	0.97	—
5 minutes	1.75	1.00	4.69	.98	5.51	1.09
10 minutes	2.23	0.98	4.59	.95	5.44	1.01
15 minutes	2.69	1.00	4.56	.98	5.52	1.01
20 minutes	2.61	0.97	4.60	.96	5.52	1.01
25 minutes	2.99	0.96	4.60	.96	5.49	1.04
30 minutes	2.74	0.98	4.56	.96	5.55	1.18
After one stir	2.4	2.00	4.83	1.08	5.50	1.49
After second stir	1.79	1.00	5.22	1.50	5.46	2.71
After vigorous stir	5.70	6.00	4.79	4.78	5.01	5.01
+ 5 minutes	6.46	6.46	4.80	4.79	—	—

sodium citrate, but vigorous stirring was necessary to provide a substantial rise in pH.

MMT behaved differently, with no neutralisation of acid without vigorous stirring, even after 30 minutes. It took 5 minutes longer for pH changes to be complete.

Discussion

Many antacids have been used to raise intragastric pH as prophylaxis against acid aspiration syndrome. The work of Vandam[6] Teabeut[7] and Roberts and Shirley[1] established guidelines to reduce the risks, and recommended that a pH of greater than 2.5 and a gastric volume of less than 25 ml be aimed at; these figures were established by experiments on rabbits and monkeys. Taylor[8] later suggested a minimum pH of 3.5, after he recorded an incident of pulmonary aspiration syndrome with a gastric pH less than 3.5, but more than 2.5.

Magnesium trisilicate mixture has remained the most common antacid used, probably because it was the first to be widely introduced. Sodium citrate solution is now gaining popularity because of concern about MMT. Sodium citrate and Alka Seltzer, non-particulate antacids, both mixed much more easily than MMT and, thus, mixing started even before agitation. This confirms the findings of Holdsworth and his colleagues,[9] who showed that MMT mixed poorly and that all antacids require that the patient move around to ensure adequate mixing in the stomach.

MMT was able to neutralise gastric acid contents, perhaps with a larger capacity than other antacids, but there remains a question regarding its effects in the lungs. Aspirated, unchanged, particulate antacids have greater adverse effects than non-particulate antacids, but it is difficult to be categorical about MMT. Heaney and Jones[10] reported two cases of aspiration pneumonitis, one of whom definitely regurgitated MMT and may have aspirated gastric contents, but eventually recovered. Gibbs and Wynne[11] claim that MMT would behave in a similar fashion to other particulate antacids, which increase physiological shunting and pulmonary vascular resistance. Peppermint oil in MMT has undesirable pharmacological actions, in that it lowers the lower oesophageal sphincter tone, thus increasing the chances of reflux.[12] This alone would cast a shadow on its use for the prophylaxis of acid aspiration. Also, many patients find MMT distasteful; it may cause nausea and vomiting, resulting in poor compliance, even in the labour ward.[13]

Sodium citrate is certainly more miscible, but is slightly more expensive than MMT, and requires aniseed or syrup to disguise its flavour.[14] Many pharmacies place a short time limit on the expiry date for sodium citrate, which may be because of interaction with the atmosphere, crystallising of the syrup, or interaction with silica in the glass of the container. Sodium citrate can be sealed in glass containers which ensure storage for 8 weeks.[4]

Alka Seltzer tablets contain 958 mg of sodium bicarbonate (approximately 11.4 mM), 312 mg potassium bicarbonate (3.1 mM), and 832 mg of citric acid (4.3 mM). Our measurements show the solution consistently has a pH of 6.5. At 20°C, the pKa of the three proton donor sites of citric acid are respectively 3.14, 4.77, and 6.34,[15] so that the first two sites are ionised and most of the third at the pH of Alka Seltzer solution. Thus, the citric acid is in solution as citrate, a potent buffering ion. Examination of the molar quantities also shows that there is sufficient bicarbonate to 'neutralise any hydrogen ions present in the citric acid.

Sodium citrate contains 18 mM sodium/20 ml dose,[16] MMT 18.9 mM/30 ml dose[17] and Alka Seltzer 23 mM/two tablet dose, so the difference in sodium content is small. Palatability of Alka Seltzer solution in pregnant mothers has not been assessed, but as it already sells directly to the consumer in the USA, it is likely to be acceptable. Theoretical expectations have been confirmed in the dog lung that Alka Seltzer Effervescent has little effect on the lung,[5] and so may be an improvement. Alka Seltzer has adequate neutralising ability, provided two tablets are used, and it is unimportant how long the solution stands (up to 30 minutes), as long as effervescence has ceased. This would also prevent carbon dioxide being generated in the stomach which, theoretically at least, might increase intragastric pressure. Individual packaging means a higher initial outlay (2.00 US dollars per box of 36 tablets USA or 11p a dose), but since it has a long shelf life there should be little waste. If it were administered immediately before Caesarean section, then its palatability, and rapid mixing would bestow definite advantages over MMT.

Further investigation is justified to assess the palatability of Alka Seltzer to pregnant mothers and its efficacy compared to other antacids prior to Caesarean section.

Acknowledgments

We wish to thank Mrs Marie Taff and Miles Laboratories for supplying the drugs and Miss D. Price for her secretarial assistance.

References

1. Roberts RB, Shirley MA. Reducing the risk of acid aspiration during Cesarian section. *Anesthesia and Analgesia* 1974; **53:** 859–68.
2. Gibbs CP, Schwartz DJ, Wynne JW, Hood CI, Kuck EJ. Antacid pulmonary aspiration in the dog. *Anesthesiology* 1979; **51:** 380–5.
3. Crawford JS, Potter SR. Magnesium trislicate mixture B.P. Its physical characteristics and effectiveness as a prophylactic. *Anaesthesia* 1984; **39:** 535–9.
4. Abouleish E, Schenle IA. Efficacy of antacid therapy. *British Journal of Anaesthesia* 1977; **49:** 394.
5. Chen CT, Toung TJ, Haupt HM, Hutchins GM, Cameron JL. Evaluation of the efficacy of Alka Seltzer effervescent in gastric acid neutralization. *Anesthesia and Analgesia* 1984; **63:** 325–9.
6. Vandam LD. Aspiration of gastric contents in the operative period. *New England Journal of Medicine* 1965; **273:** 1206–8.
7. Teabeaut JR. II Aspiration of gastric contents, experimental study. *American Journal of Pathology* 1952; **28:** 51–67.
8. Taylor G. Acid pulmonary aspiration syndrome after antacids. A case report. *British Journal of Anaesthesia* 1975; **47:** 615–6.
9. Holdsworth JD, Johnson K, Mascall G, Gwynne Roulston R, Tomlinson PA. Mixing of antacids with stomach contents. Another approach to the prevention of the acid aspiration (Mendelson's) syndrome. *Anaesthesia* 1980; **35:** 641–50.
10. Heaney GAH, Jones HD. Aspiration syndromes in pregnancy. *British Journal of Anaesthesia* 1979; **51:** 266–7.
11. Gibbs CP, Wynne JW. Maternal mortality and anaesthesia. *British Journal of Anaesthesia* 1980; **52:** 842.
12. Sigmund CJ, McNally EF. The action of a carminative on the lower esophageal sphincter. *Gastroenterology* 1969; **56:** 13–18.
13. Duffy BL, Woodhouse PC. Sodium citrate and gastric acidity in obstetric patients. *Medical Journal of Australia* 1982; **2:** 37–8.
14. Lahiri SK, Thomas TA, Hodgson RMH. Single dose antacid therapy for the prevention of Mendleson's syndrome. *British Journal of Anaesthesia* 1973; **45:** 1143.
15. Sober HA. Ed, C.R.C. *Handbook of Biochemistry*, 2nd edn, 1973. Cleveland Ohio: C.R.C. Press.
16. Reynolds JF. Ed, *Martindale. The extra Pharmacopeia* 28th edn 1982. London: The Pharmaceutical Press.
17. Barry RE, Ford J. Sodium content and neutralizing capacity of some commonly used antacids. *British Medical Journal* 1978; **1:** 413.

Anaesthesia, 1986, Volume 41, pages 143–147

Continuous infusion epidural analgesia in obstetrics

A comparison of 0.08% and 0.25% bupivacaine

A. EWEN, D. D. McLEOD, D. M. MacLEOD, ALISON CAMPBELL AND M. E. TUNSTALL

Summary

The effects of 0.08% (Group A) and 0.25% (Group B) solutions of bupivacaine were compared in a random manner, to assess continuous pump infusion epidural analgesia in labour. Both solutions were infused at a dose rate of 20 mg bupivacaine/hour. The results in all the mothers who had received infusions lasting more than 4 hours were studied. There were 25 in Group A and 28 in Group B. Any treatment during the infusion epidural for inadequate analgesia, hypotension, etc., was recorded as an intervention. The mean of the intervention-free intervals was significantly greater in Group A than in Group B, and significantly fewer top-up injections were required in Group A. The results show that the administration of a 0.08% solution of bupivacaine into the epidural space by continuous pump infusion is more labour saving than the infusion of a 0.25% solution. The concept that a greater volume infusion rate maintains a more extended liquid sleeve of local anaesthetic in the epidural space is supported.

Key words

Anaesthetic techniques, regional; epidural.
Anaesthetics, local; bupivacaine.

Maintenance of epidural analgesia by continuous pump infusion of local anaesthetic into the epidural space has been shown to be effective and safe, and to offer advantages over intermittent top-up procedures.[1,2] The main advantages for the patient are uninterrupted analgesia and greater safety. For the anaesthetist there is less requirement for time consuming top-up injections.

Concentrations selected for infusion epidurals have ranged from 0.0625% to 0.375%, at dose rates from 6.25 mg to over 20 mg/hour of bupivacaine.[1–5] Recently, it has been shown that a solution of bupivacaine at a concentration of 0.08% infused at 25 ml/hour is able to provide long periods of uninterrupted analgesia in labour.[6] Sixty per cent of the mothers required no supplementary top-ups. It was proposed that increasing the volume infused extended the liquid sleeve of local anaesthetic in the epidural space and caused more dermatomes to remain blocked. The aim of the present study was to see if there was any support for this concept, and to test whether the more dilute solution was more labour-saving.

The use of continuous infusion epidurals with

A. Ewen*, MB, ChB, FFARCS, Registrar, D.D. McLeod, MB, ChB, FFARCS, Senior Registrar, D.M. MacLeod, MB, ChB, FFARCSI, Registrar, A. Campbell, MB, ChB, Registrar, M.E. Tunstall, MB, BS, FFARCS, Consultant, Department of Anaesthetics, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB9 2ZB.

Correspondence should be addressed to Dr M.E. Tunstall, Aberdeen Maternity Hospital, Cornhill Road, Aberdeen AB9 2ZA.

*Present appointment: Senior Registrar, Guy's Hospital, London SE1.

0003–2409/86/020143 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

0.08% bupivacaine had been established in Aberdeen, but individual members of the department continued to use 0.25% solutions of bupivacaine. They were not convinced there was any great advantage in making up a more dilute solution. It was therefore decided to compare 0.08% and 0.25% solutions of bupivacaine in a controlled manner. The existing dose rate of 20 mg/hour was chosen. If the more dilute solution maintained a wider segmental blockade, then one would expect that fewer top-ups would be required. This would support the liquid sleeve concept and also show that the more dilute solution was relatively labour-saving.

Method

The obstetric population in Aberdeen to whom epidural analgesia is available is approximately 4000 per annum. Approximately 1000 normal mothers per annum are delivered in nearby satellite maternity homes within the city where epidural analgesia is not available. The overall epidural rate is about 20%. Midwives in Aberdeen have never been allowed to administer top-up injections into the epidural space, nor have they been allowed to control the rate of infusion epidurals. They are allowed to switch off epidural infusions when indicated, position patients in the treatment of hypotension, and call the anaesthetist.

The subjects of the present investigation were from a consecutive series of mothers who were to receive epidural analgesia during labour at the Aberdeen Maternity Hospital within a 4-week period. The subjects were randomly allocated to two groups, A and B. Group A was to receive 0.08% bupivacaine (without adrenaline) at 25 ml/hour and Group B was to receive 0.25% bupivacaine (without adrenaline) at 8 ml/hour. In the subsequent assessment, the results of all mothers who had received infusions of less than 4 hours duration were not included. Within this period, it was considered that the initial induction dose of bupivacaine would have a dominant effect.

Technique

After a slow intravenous infusion of crystalloid had been initiated via a large bore cannula, epidural analgesia was induced with the patient in the left lateral decubitus position, using a 16G Tuohy needle. All epidurals were inserted in the L_{3-4} interspace, although the choice of midline or paramedian approach was left to the individual anaesthetist. A Portex epidural catheter was advanced 4 cm into the epidural space, and connected to a Millipore bacterial filter. After negative aspiration for blood or cerebrospinal fluid (CSF), a test dose of 3 ml of 0.5% bupivacaine plain was injected. The catheter was then secured to the skin with a waterproof adhesive dressing and the patient turned to a position of left lateral tilt. Having confirmed no untoward sequelae from the test dose, a further 8 ml of 0.5% bupivacaine plain was injected and the blood pressure was checked every minute for the next 5 minutes. During this time, the dilution of the bupivacaine solution was made. For the 0.08% solution, 48 ml of 0.5% bupivacaine plain was added to a 250 ml bag of normal saline (Boots/Steriflex). For the 0.25% solution, 50 ml from a 100 ml bag of normal saline was replaced by 50 ml of 0.5% bupivacaine plain. The infusion bag was connected via a standard infusion administration set (Avon A100) to a volumetric infusion pump (Imed 960) with administration cassette (Accuset C-924). The occlusion alarm on the infusion pump had been reset by the Department of Medical Physics to alarm at a higher pressure than normally set; this was found to be desirable when using the higher infusion rate. The connexion from pump to Millipore filter was completed by a three-way tap which allowed for top-up injections and the infusion was commenced at the appropriate rate.

Observations

After the infusion was started, each subject was reviewed by the anaesthetist every 2 hours. Observations were made about the degree of sensory block, identified by loss of temperature sensation to ice and about the degree of motor block, measured as 0: no leg weakness; 1: minimal leg weakness (able to lift the foot off the bed); 2: moderate leg weakness (able to slide the foot up the bed); 3: severe leg weakness (unable to slide the foot up the bed). Arterial blood pressure was measured by the midwife using a standard sphygmomanometer. Measurements below 100 mmHg systolic were recorded as episodes of hypotension. The subjects in both groups were asked to describe any periods of pain under the following headings: no pain; insignificant pain; painful but bearable; unbearable.

Interventions

If the anaesthetist was called at any time to see the patient, because of either inadequate analgesia or a side effect, the event was recorded as an intervention. Any treatment given or adjustment made by the anaesthetist during the time of the regular 2-hourly assessment was also recorded as an intervention.

Analysis of the results

Student's t-test for unpaired samples and Fisher's exact test were used.

Results

Fifty-three subjects were included in the study. Twenty-five of these received 0.08% bupivacaine (Group A), and twenty-eight received 0.25% bupivacaine (Group B). All patients in whom the duration of the infusion was less than 4 hours had already been excluded. There were no significant differences between the two groups with respect to age, weight, height and parity (Table 1).

The mean duration of the epidural infusions was 481 minutes in Group A and 458 minutes in Group B. In Group A there were 47 intervention-free intervals and in Group B there were 73. The mean duration of the intervention-free intervals was significantly longer in Group A. The longest individual intervention-free interval for each mother was divided by the total infusion time and expressed as a ratio. The mean value of these ratios was significantly greater for Group A mothers (Table 2).

There were significantly fewer interventions in Group A compared to Group B in mothers requiring treatment (Table 3). Significantly fewer mothers required top-ups in Group A than in Group B (Table 4). Total bupivacaine dosage given as bolus injections (initial dose plus top-ups) was significantly less in Group A mothers (Table 5). There was a significantly greater incidence of severe leg weakness in Group A than in Group B (Table 6). There were 12 hypotensive episodes in Group A and five in Group B. Four of the episodes in Group A and two in Group B were not related to initial or top-up injections (Table 7). There was one case of mild inter-

Table 2. Duration of epidural infusions and intervention-free intervals. Mean (SEM)

	Group A	Group B
Duration of infusion (minutes) x	481(44)	458(37)
Duration of all intervention-free intervals (minutes)	250(29)	176(17)*
Duration of the longest intervention-free interval for each mother minutes) y	389(33)	304(29)
y/x ratios	0.834(0.04)	0.708(0.05)†

*$p<0.025$; †$p<0.05$.
N.B. Where no intervention has been required during the epidural infusion, the intervention-free interval equals the duration of the infusion. In such a case the y/x ratio = 1.

Table 3. Interventions during continuous pump infusion epidural

Interventions	Group A	Group B
Number of mothers requiring one or more	16	20
Number of mothers requiring none	9	8
Mothers requiring interventions		
Number of interventions per mother (mean, SEM)	1.5 (0.22)	2.35 (0.33)*

*$p<0.05$.

Table 4. Top-up injections required for maintenance of analgesia during continuous pump infusion epidural

Top-ups	Group A	Group B
Number of mothers requiring one or more	10	19
Number of mothers requiring none	15	9
Number of top-ups per mother (mean, SEM)	0.6(0.17)	1.32(0.22)*

*$p<0.02$.

Table 1. Patient data in the two groups

	Number of mothers		Mean (SEM)		
Group	Primip	Multip	Age	Weight (kg)	Height (cm)
A	22	3	25.1 (0.73)	74.6 (1.93)	161.3 (0.85)
B	23	5	25.9 (0.84)	76.1 (1.86)	158.8 (1.42)

Table 5. Bupivacaine dosage received by the mothers (mean, SEM)

Total of initial bolus plus top-up injections only (mg)	
Group A	77 (6.0)
Group B	110 (9.9)*
Total bupivacaine dosage (mg, including infusion)	
Group A	232 (16.7)
Group B	261 (16.5)

*<0.01.

Table 6. Leg weakness

	Number of mothers				
	Group A		Group B		
Maximum leg weakness score	Right leg	Left leg	Right leg	Left leg	
0	1	1	2	3	
1	6	7	8	8	
2	6	7	12	12	
3	12	10	6	5	
Total number of legs at scores 0–2	28		45		*
Total number of legs at score 3	22		11		

*$p<0.012$ (Fisher's exact test).

Table 7. Hypotensive episodes

	Time in minutes after the start of the epidural infusion	
	Group A	Group B
1st episode	(35)	100
	(10)	70
	(30)	(15)
	(20)	(15)
	(0)	
	(5)	
	75	
	(15)	
	(0)	
2nd episode	60	(400)
	230	
3rd episode	290	

Times in parentheses indicate hypotensive episodes related to top-up injections.

scapular pain in Group A. Shivering occurred in one Group A and in three Group B mothers. Bilateral segmental analgesia above T_4 occurred in eight mothers in Group A and in five mothers in Group B.

In the post delivery interview, mothers were asked to recall any periods of pain during the epidural infusion and grade the one which was most severe. The results are shown in Table 8. On direct questioning of each mother, only one in Group A and five in Group B stated that leg weakness bothered them. The five in Group B were bothered 'only a little', while the one in Group A was bothered 'a lot'. This mother was also the only one who said she would not have an epidural again.

Mode of delivery is shown in Table 9. One mother in Group A and two in Group B had Caesarean sections under the effects of the continuous epidural without supplement by a top-up.

Table 9. Mode of delivery in the two groups

Group	Spontaneous vaginal	Forceps	Caesarean section
A	5	16	4
B	2	16	10

Discussion

The results of this study show a greater effectiveness of the 0.08% solution in maintaining satisfactory analgesia. It has already been shown that milligram for milligram of bupivacaine, a stronger solution is less effective than a more dilute solution during continuous pump infusion epidurals.[7] In a recent clinical investigation,[5] it was stated that the optimum infusion rate for this form of epidural was 0.125% bupivacaine at 10 ml/hour. Nineteen of the mothers received that dose rate and dilution for periods longer than 3 hours. Only four of them did not require top-ups. In the 25 mothers in Group A, where the

Table 8. Mothers' assessment of the worst period of pain during the epidural infusion

	Maximum severity of pain			
Group	No pain	Insignificant	Bearable	Unbearable
A	11	8	5	1
B	6	9	10	3

epidural infusion period was always in excess of 4 hours and the mean duration greater, 15 of the mothers did not require top-ups.

An infusion dosage of 20 mg/hour bupivacaine should rarely need to be exceeded for the maintenance of satisfactory analgesia. In a different population and obstetric environment, satisfactory results have been reported with 12.5 mg/hour bupivacaine, in a 0.25% solution, with the epidural catheter inserted into the L_1–L_2 interspace.[8] There is a risk involved in the choice of a high lumbar interspace, as it is near the termination of the spinal cord. One of the objectives of the low dose rate delivered at a high lumbar level was to reduce instrumental delivery, and the incidence was a third of that in the present study. The mothers in Aberdeen, however, once the epidural has been successfully established, generally wish the pain relief to remain complete throughout labour.

Hypotension may complicate the administration of a bolus dose of bupivacaine. Reduction of top-up epidural injections may be expected to reduce the incidence of hypotension during the course of the epidural. Most of the hypotensive episodes in the present study were related to bolus injections into the epidural space.

Complications due to delayed or unrecognised perforation of the dura by the catheter are likely to be revealed in a less dramatic manner with a continuous pump infusion epidural using a dilute solution of bupivacaine than with an intermittent top-up technique with 0.5% bupivacaine. In addition, the 0.08% solution should have the advantage of giving warning of intrathecal infusion earlier than the 0.25% solution, because of the greater volume infused. One would expect a block which would be differential; that is to say despite paraesthesia reaching the upper thoracic dermatomes, ventilatory activity would remain unimpaired. This observation is commonly made during spinal anaesthesia with an isobaric solution of 15 mg of bupivacaine. Another theoretical consideration is that the 0.25% solution might remain localised in the lumbar area during slow intrathecal injection. Sudden cephalad spread of the solution might occur when the patient changes position.[9]

Except for rapidly progressing labours, or requests for epidural analgesia made late in labour, we would recommend setting up continuous pump infusion epidurals with 0.08% bupivacaine as a matter of course.

Acknowledgments

We wish to thank Dr G.P. Ramayya FFARCS, Registrar in the Department of Anaesthetics, Aberdeen Royal Infirmary, for the use of his computerised obstetric data filing system and Mrs Audrey Gordon who typed the manuscript.

References

1. Evans KRL, Carrie LES. Continuous epidural infusion of bupivacaine in labour: a simple method. *Anaesthesia* 1979; **34:** 310–5.
2. Davies AD, Fettes IW. A simple safe method for continuous infusion epidural analgesia in obstetrics. *Canadian Anaesthetists' Society Journal* 1981; **28:** 484–7.
3. Glover DJ. Continuous infusion epidural analgesia in the obstetric patient: a feasibility study using a mechanical infusion pump. *Anaesthesia* 1977; **32:** 499–503.
4. Taylor HJC. Clinical experience with continuous epidural infusion of bupivacaine at 6 ml per hour in obstetrics. *Canadian Anaesthetists' Society Journal* 1983; **30:** 277–85.
5. Li DF, Rees GAD, Rosen M. Continuous extradural infusion of 0.0625% or 0.125% bupivacaine for pain relief in primigravid labour. *British Journal of Anaesthesia* 1985; **57:** 264–70.
6. Tunstall ME, Ramamoorthy C. Continuous epidural infusion with 0.08% bupivacaine. *Anaesthesia* 1984; **39:** 939–40.
7. Kenepp NB, Cheek TG, Gutsche BB. Bupivacaine: continuous infusion epidural analgesia for labor. *Anesthesiology* 1983; **59:** A407.
8. Matouskova A, Hanson B, Elmén H. Continuous mini-infusion of bupivacaine into the epidural space during labour. Part III: A clinical study of 225 parturients. *Acta Obstetrica et Gynecologica Scandinavica* 1979; Suppl. **83:** 43–52.
9. Russell IF. Inadvertent total spinal for Caesarean section. *Anaesthesia* 1985; **40:** 199–200.

Anaesthesia, 1986, Volume 41, pages 148–150

Bacterial contamination of compressed air for medical use

P. BJERRING AND B. ØBERG

Summary

The present study demonstrates a previously unnoticed source of bacterial contamination of locally manufactured compressed air for medical use. Air samples were drawn into a specially constructed device, and bacterial contents were identified from growth on agar plates. Various factors contributing to bacterial contamination of compressed air during production are mentioned and preventive measures are discussed.

Key words

Equipment; compressed air.
Contamination; bacterial.

During the last 25 years, a number of authors have investigated respiratory tract colonisation by bacteria, in patients undergoing anaesthesia or ventilator treatment in operating rooms and intensive care units (ICU). These investigators, however, have focussed exclusively on the aetiological role of ventilator tubing,[1,2] humidifiers,[3] anaesthetic apparatus,[4-7] mechanical ventilators,[8] resuscitation apparatus,[9] and lack of clinical cleanliness by medical and nursing staff.[10] The aim of the present study was to determine whether air compressors, air storage tanks, pipelines and connectors might be incriminated as sources of microbial contamination. To our knowledge, no investigators have dealt with possible contamination of compressed air.

Air for medical use (ÀM, Aer Medicinalis) is manufactured locally, in the hospital's Technical Department and has to meet certain quality requirements specified in the Pharmacopoeia Nordica,[11] but these regulations deal with the chemical composition only. Surprisingly, no limitations are laid down for any possible microbial contamination, nor does the International Standards Organisation have any recommendations.

Methods

Air samples were collected into a specially constructed device, from pipeline outlets in operating rooms and ICUs throughout the hospital. During each period of sampling, 18 litres of air/minute were drawn into a Bourdillon slit sampler[12] in which a 14 cm Petri dish (10% blood agar) was slowly rotating. During the 10 minute sampling time, the turntable holding the Petri dish rotated once. The construction of the slit sampler ensured close contact between the air samples and Petri dishes. Prior to each sampling, all accessible parts of the device were carefully cleaned with 62% ethanol and the

---

P. Bjerring, MD, Resident, Department of Dermatology, Marselisborg Hospital, B. Øberg, MD, Resident, Department of Anaesthesia, Aarhus Kommunehospital, DK-8000 Aarhus, Denmark.

Correspondence should be addressed to Dr B. Øberg, Department of Anaesthesia, Aarhus Kommunehospital, DK-8000 Aarhys, Denmark please.

0003–2409/86/020148 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Micro-organisms found in central air compressors and peripheral air outlets

Contaminants	Central ($n = 7$)	Peripheral ($n = 27$)	
	Number of plates with the micro-organism (%)	Number of plates with the micro-organism (%)	Average number of micro-organisms in positive samples/1000 litres of air
Pseudomonas aeruginosa	2 (29)	0 (0)	–
Staphylococcus albus	2 (29)	16 (59)	9
Corynebacterium species	1 (14)	3 (11)	10
Micrococcus species	0 (0)	5 (19)	9
Bacillus species	1 (14)	8 (30)	6
Moulds	1 (14)	5 (19)	16
Plates without growth	2 (29)	5 (19)	
Percent positive samples	71	81	

whole system was flushed with the air to be collected, at a rate of 65 litres/minute. Samples were also drawn from a sterile laminar flow cabinet to provide negative controls. The Petri dishes were then submitted to the Regional Department of the Danish State Serum Institute for culture and identification of bacteria and fungi.

Specimens of condensed water were also taken from the compressed air storage tanks in the hospital's technical department which supplied the investigated peripheral outlets. Bacterial and fungal contamination was again determined from growth on agar plates.

Results

Table 1 lists the micro-organisms. A total of 34 samples were analysed, seven from central installations and 27 from peripheral air outlets. In positive samples, the number of micro-organisms varied from 6 to 16/1000 litres of air. No other contaminants were found, other than the above mentioned micro-organisms.

Discussion

The results show a previously unnoticed source of infectious agents. A possible explanation for apparently uncontaminated plates may well be impaction of bacteria between the air intake and the slit sampler, and inability of the slit sampler to trap all bacteria present. The values in Table 1 must therefore be minimum figures, and the problem is undoubtedly underestimated in this study.

Other investigators have examined anaesthetic systems after use[13] or storage[2] and demonstrated a possible route of infection from patient to patient. This, indeed, is of great significance, and has resulted in numerous methods of disinfection of anaesthetic apparatus and ventilators.[14–16] It is equally important, however, that patients in ICUs and postoperative patients may be exposed to pathogens via high-flow air–oxygen mixtures (Y-systems) or ventilator systems. Even if the presence of bacteria in the inspired air does not necessarily mean that patients will become infected, it certainly increases the likelihood of that event.

The bacterial flora isolated from peripheral air outlets, which in our investigation is virtually the same as that found in the central air-generating installations, is a mixture of pathogens and normal skin bacteria. However, when supplied directly into the tracheas of seriously ill patients, no sharp distinction between pathogenic and non-pathogenic bacteria can be maintained. Furthermore, the mucociliary transport system may be impaired by high oxygen tensions in the inspired air,[17] or by drugs such as atropine[18] acetylsalicylic acid[19] and morphine.[20] The stagnation of bronchial secretions is a well-known complication in ICU patients, and the presence of bacteria in air inspired via a tracheal tube may add to the problem. Whereas a general medical or surgical patient has a 6% risk of becoming infected during his hospital stay, the ICU patient has an 18% risk.[21]

Air for medical use is rich in condensed water, and the oil aerosol from the compressor makes air storage tanks favourable media for the proliferation of bacteria. In the present investigation, *Pseudomonas aeruginosa* were found in oil–water emulsions from AM storage tanks. Oil–water aerosols may also cover the inner surfaces of the pipeline system and act as a growth medium for micro-organisms. In extensive pipeline systems, special attention must be paid to blind loops and other locations suitable for trapping and proliferation of bacteria.

The source of the bacteria is either the lubricating oil for the compressors or the ambient air being taken into the compressors without interposition of a bacterial filter. The solutions to this problem would be the use of sterile oil, reduction of oil in the AM, and the addition of bacterial filters to the compressors' air intakes. Inhalation by patients of mineral oil aerosol contained in AM is limited to 5 mg/cu m air;[11] whether long term exposure to such aerosols during ventilator treatment may lead to lipid pneumonia remains an unsolved problem.

Until sterile air can be supplied, we also recommend filters in ventilators and all other equipment driven by or requiring AM, but the efficiency of bacterial filters contaminated with oil must be questioned. Users of AM, as well as producers (Hospital Authorities), are urged to focus on this possible source of bacterial contamination of seriously ill patients receiving different types of ventilatory assistance.

It may be necessary to set limits to the maximum bacterial content of medical air. Regular quality control by Health Authorities must prevent the air from being a constant source of bacterial contamination, which would otherwise significantly reduce the value of sterilisation efforts directed at equipment closer to the patient. Medical air is a pharmaceutical specialty, registered in the pharmacopoeias, and the usual high standard of quality control should include this product as well..

Acknowledgments

The authors are indebted to Dr med. P. Bülow, Regional Department of the Danish State Serum Institute in Aarhus for contributing his microbiological expertise, and to Professor, Dr med. B. Juhl, Department of Anaesthesiology, Aarhus University Hospital for helpful discussions and critical revision of the manuscript.

References

1. CRAVEN DE, CONNOLLY MG, LICHTENBERG DA, PRIMEAU PJ, MCCABE WR. Contamination of mechanical ventilators with tubing changes every 24 or 48 hours. *The New England Journal of Medicine* 1982; **306:** 1505–9.
2. IM SWK, FUNG JPH, SO SY, YU DYC. Unusual dissemination of pseudomonads by ventilators. *Anaesthesia* 1982; **37:** 1074–7.
3. DONS N, ERIKSEN KR, JØRGENSEN S. An oxygen therapy apparatus as a source of infection. *Ugeskrift for Laeger* 1959; **121:** 1525–8.
4. NIELSEN H, VASEGAARD M, STOKKE DB. Bacterial contamination of anaesthetic gases. *British Journal of Anaesthesia* 1978; **50:** 811–4.
5. NIELSEN H, JACOBSEN JB, STOKKE DB, BRINKLØV M, CHRISTENSEN KN. Cross-infection from contaminated anaesthetic equipment. A real hazard? *Anaesthesia* 1980; **35:** 703–8.
6. FEELEY TW, HAMILTON WK, XAVIER B, MOYERS J, EGER EI. Sterile anesthesia breathing circuits do not prevent postoperative pulmonary infection. *Anesthesiology* 1981; **54:** 369–72.
7. GARIBALDI RA, BRITT MR, WEBSTER C, PACE NL. Failure of bacterial filters to reduce the incidence of pneumonia after inhalation anesthesia. *Anesthesiology* 1981; **54:** 364–8.
8. COMHAIRE A, LAMY M. Contamination rate of sterilized ventilators in an ICU. *Critical Care Medicine* 1981; **9:** 546–8.
9. DREWETT SE, PAYNE DJH, TUKE W, VERDON PE. Eradication of *Pseudomonas Aeruginosa* infection from a special-care nursery. *Lancet* 1972; **1:** 946–8.
10. TERES D, SCHWEERS P, BUSHNELL LS, HEDLEY-WHYTE J, FEINGOLD DS. Sources of *Pseudomonas Aeruginosa* infection in a respiratory/surgical intensive-therapy unit. *Lancet* 1973; **1:** 415–7.
11. *Pharmacopoea Nordica* 1963 Addendum. Aer Medicinalis.
12. BOURDILLON RB, LIDWELL OM, LOVELOCK JE. Studies in air hygiene. *Microbiology Research Council Special Report Series*, London 1948. No. 262.
13. PANDIT SK, MEHTA S, AGARWAL SC. Risk of cross-infection from inhalation anaesthetic equipment. *British Journal of Anaesthesia* 1967; **39:** 838–44.
14. BISHOP C, POTTS MW, MOLLOY PJ. A method of sterilization for the Barnet respirator. *British Journal of Anaesthesia* 1962; **34:** 121–3.
15. SYKES MK. Sterilizing mechanical ventilators. *British Medical Journal* 1964; **1:** 561.
16, STRATFORD BC, CLARK RR, DIXON S. The disinfection of anaesthetic apparatus. *British Journal of Anaesthesia* 1964; **36:** 471–6.
17. SACKNER MA, HIRSCH JA, EPSTEIN S, RYWLIN AM. Effect of oxygen in graded concentrations upon tracheal mucous velocity. A study in anesthetized dogs. *Chest* 1976; **69:** 164–7.
18. ANNIS P, LANDA J, LICHTIGER M. Effects of atropine on velocity of tracheal mucus in anesthetized patients. *Anesthesiology* 1976; **44:** 74–7.
19. GERRITY TR, COTROMANES E, GARRARD CS, YEATES DB, LOURENCO RV. The effect of aspirin on lung mucociliary clearance. *The New England Journal of Medicine* 1983; **308:** 139–41.
20. FORBES AR, HORRIGAN RW. Mucociliary flow in the trachea during anesthesia with enflurane, ether, nitrous oxide, and morphine. *Anesthesiology* 1977; **46:** 319–21.
21. DONOWITZ LG, WENZEL RP, HOYT JW. High risk of hospital-acquired infection in the ICU patient. *Critical Care Medicine* 1982; **10:** 355–7.

Anaesthesia, 1986, Volume 41, pages 151–154

Time course of action of combinations of vecuronium and pancuronium

S. K. PANDIT, C. J. FERRES, F. M. GIBSON AND R. K. MIRAKHUR

Summary

Vecuronium 0.1 mg/kg, pancuronium 0.1 mg/kg, vecuronium 0.075 mg/kg + pancuronium 0.025 mg/kg, vecuronium + pancuronium 0.05 mg/kg each and vecuronium 0.025 mg/kg + pancuronium 0.075 mg/kg were compared with respect to time taken to onset of effect, duration of clinical relaxation and intubation conditions in five groups of 20 patients each. The time to onset and intubating conditions were similar in all the groups, indicating that the combinations have no advantage over the individual drugs. The duration of clinical relaxation was 25 minutes with vecuronium, and increased as the proportion of pancuronium in the mixture increased, being 56 minutes with pancuronium 0.1 mg/kg.

Key words

Neuromuscular relaxants; pancuronium, vecuronium.

Of all the currently available muscle relaxants, only suxamethonium provides quick and profound muscle relaxation for a relatively short period of time. Thus, despite its several disadvantages, suxamethonium remains the muscle relaxant of choice in many situations, such as those which call for a rapid sequence induction of anaesthesia and tracheal intubation as in patients presenting for emergency surgery with a full stomach. Non-depolarising muscle relaxants such as pancuronium can provide good conditions for rapid tracheal intubation only if the dose is increased much beyond the normal range.[1] However, large doses may be inappropriate in operations of a relatively short duration. The recently introduced muscle relaxant, vecuronium, is a definite improvement as it provides acceptable intubating conditions more rapidly than pancuronium, but these are still not as good as those obtained with suxamethonium.[2] It has been demonstrated that a combination of relaxants such as pancuronium plus metocurine or pancuronium plus tubocurarine is associated not only with a potentiation of effect, but also with a shorter duration of block and a slightly more rapid onset of action.[3–5]

The purpose of the present study was to assess the intubating conditions with, and to determine

---

S.K. Pandit,* PhD, FFARCS, Visiting Professor, C.J. Ferres,† MD, FFARCS, Research Fellow, F.M. Gibson, MB, FFARCS, Research Fellow, Department of Anaesthetics, The Queen's University of Belfast, R.K. Mirakhur, MD, PhD, FFARCS, FFARCSI, Consultant Anaesthetist, Royal Victoria Hospital, Belfast.

*Present address: University of Michigan Medical Center, Ann Arbor, Michigan, USA.

†Present address: Consultant Anaesthetist, Whiteabbey Hospital, Newtownabbey, County Antrim, Northern Ireland.

Correspondence should be addressed to R.K. Mirakhur please.

0003–2409/86/020151 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

the time course of action of, three different combinations of pancuronium and vecuronium, and to compare these with the commonly used standard doses of the individual drugs.

Patients and methods

One hundred adult patients 15–65 years of age, ASA grades 1 and 2, who gave informed consent, were included in the study following approval from the regional ethical committee. All were undergoing elective surgery requiring the use of non-depolarising muscle relaxants.

Following premedication with diazepam 10–15 mg orally, anaesthesia was induced with thiopentone 4–5 mg/kg and maintained with 70 percent nitrous oxide in oxygen and intravenous fentanyl 4–5 μg/kg and droperidol 2.5–5.0 mg. Ventilation was assisted as required. Vecuronium, pancuronium or three combinations of these muscle relaxants were administered as a bolus dose in the amounts and proportions shown in Table 1. Twenty patients were randomly allocated to each of the five groups.

Table 1. Muscle relaxant dosage

Group	Drugs	Dosage (mg/kg)	*n*
I	Vecuronium	0.1	20
II	Vecuronium + pancuronium	0.075 0.025	20
III	Vecuronium + pancuronium	0.05 0.05	20
IV	Vecuronium + pancuronium	0.025 0.075	20
V	Pancuronium	0.1	20

Intubating conditions at 60 seconds after relaxant administration were assessed on a four point scale as excellent, satisfactory, fair or poor, using previously described criteria.[2,6] Excellent and satisfactory grades are considered clinically acceptable; a grade of poor indicates failure to intubate.

A peripheral nerve stimulator (Myotest, Biometer Ltd) delivering a train-of-four (TOF) stimulation at 2 Hz every 10 seconds to the ulnar nerve at the wrist using surface electrodes was used to monitor the neuromuscular block. The number of contractions felt in response to the TOF stimulation were counted with the thumb held in slight abduction. The onset of complete block was taken as the time from the administration of the relaxant to the time at which all four responses to a TOF stimulation disappeared. The duration of clinical relaxation was taken as the time from drug administration to the reappearance of all four responses. Though this tactile method of assessing neuromuscular block is not the most accurate,[7] it is useful for its simplicity as it does not involve the use of a transducer and recording system. Moreover, the end points used in the study would perhaps not be affected. The study was terminated at this point and further anaesthesia and muscle relaxation maintained according to the subsequent needs of surgery. Heart rate and arterial blood pressure were monitored throughout using ECG and a Dinamap.

The comparability of ages and weights was assessed using analysis of variance, as were the times to onset and duration of clinical relaxation. Intubating conditions were compared using the Chi squared test.

Results

The physical characteristics of the patients in the various groups are given in Table 2. There are no significant differences in ages ($F = 1.98$, $p > 0.05$) and weights ($F = 0.12$, $p > 0.05$). Females represent a majority in all groups.

Table 2. Physical characteristics of patients

Group	Mean age years (SEM)	Mean weight kg (SEM)	Sex M	F
I	37 (2.4)	62 (2.8)	3	17
II	42 (2.7)	62 (2.4)	4	16
III	45 (2.9)	61 (2.4)	4	16
IV	39 (2.5)	62 (2.1)	2	18
V	36 (2.6)	63 (2.1)	6	14

Differences between groups not significant.

The intubating conditions obtained in the various groups are shown in Fig. 1. Only about half the intubations were clinically acceptable across the groups and there were no significant differences in the groups in this respect ($\chi^2 = 5.05$, $df = 4$, $p > 0.05$). The time to onset of maximum block (shown in Table 3) varied from 3.4 to 4.0 minutes; the difference between the groups was insignificant ($F = 0.89$, $p > 0.05$). The main difference observed between the groups was in the duration of clinical relaxation. As Fig. 2 illustrates, the duration increased steadily as the proportion of pancuronium in the mixture in-

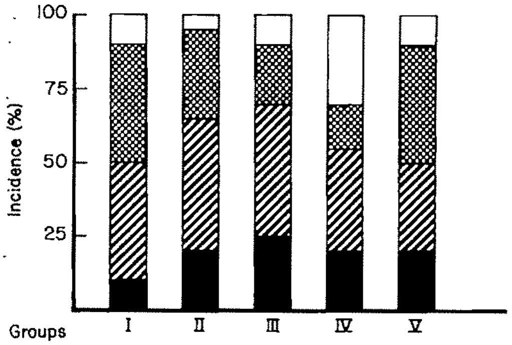


Fig. 1. Intubating conditions following administration of vecuronium and pancuronium and their combinations (see Table I for identification of groups). (■), Excellent; (■), satisfactory; (▨), fair; (☐), poor.

Table 3. Time to onset of maximum block

Group	Time minutes (SEM)
I	3.9 (0.29)
II	3.4 (0.21)
III	3.5 (0.25)
IV	3.6 (0.27)
V	4.0 (0.24)

Differences between groups not significant.

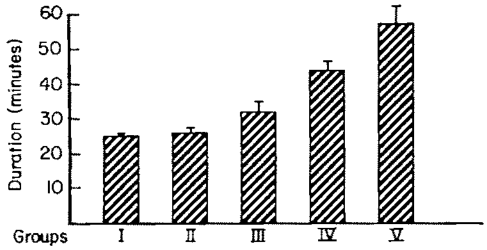


Fig. 2. Duration of clinical relaxation following vecuronium and pancuronium and their combinations (see Table I for identification of groups).

creased. The duration was 25 minutes with vecuronium alone and it increased to 26, 32, 44 and 57 minutes respectively, in Groups II to V; this was significant as tested by analysis of variance (F = 22.26, p < 0.01).

Discussion

The present study was designed not only to compare vecuronium and pancuronium, but also to study any interaction between them. It is clear that the onset of neuromuscular block is not any faster when combinations of vecuronium and pancuronium are used, in comparison to the individual relaxants. This may be due to the fact that a combination of pancuronium and vecuronium results only in a simple summation of effect, rather than any potentiation.[8] The similar time to onset of effect is also reflected in the intubating conditions, which are not significantly different from each other. It is also clear that, in general, only about 50 percent of intubations carried out at 60 seconds are clinically acceptable right across the groups. It is possible that the intubating conditions would improve if these were carried out at 90 or 120 seconds, but these would then be no better than those observed with vecuronium alone at these times.[6] Even if a dose of 0.15 or 0.2 mg/kg of vecuronium is used in an attempt to facilitate earlier intubation, this is not associated with a prolonged block, as is encountered with similar doses of pancuronium.[1]

In the present study, the duration of clinical relaxation with vecuronium was shortest amongst all the groups, averaging about 25 minutes. It increased as the proportion of pancuronium in the mixture was increased. This is in keeping with the comparative durations of action of vecuronium and pancuronium,[9] and would be expected in the absence of any potentiation.

In conclusion, it is clear from the present study that combinations of vecuronium and pancuronium do not significantly alter the time course of action of either drug and have no clinical usefulness.

References

1. Brown EM, Krishnaprasad D, Smiler BG. Pancuronium for rapid induction technique for tracheal intubation. *Canadian Anaesthetists' Society Journal* 1979; **26**: 489–91.
2. Clarke RSJ, Mirakhur RK, Bali IM, Dundee JW. Intubating conditions with Org NC 45: a comparison with suxamethonium and pancuronium. In: Prys-Roberts C. and Vickers M.D. (Eds). *Cardiovascular measurement in anaesthesiology*. European Academy of Anaesthesiology Vol. 2, Heidelberg: Springer-Verlag, 1982, pp. 86–90.
3. Lebowitz PW, Ramsey FM, Savarese JJ, Ali HH. Potentiation of neuromuscular blockade in man produced by combinations of pancuronium and metocurine or pancuronium and d-tubocurarine. *Anesthesia and Analgesia* 1980; **59**: 604–9.
4. Lebowitz PW, Ramsey FM, Savarese JJ, Ali HH, DeBros FM. Combination of pancuronium and metocurine: neuromuscular and hemodynamic advantages over pancuronium alone. *Anesthesia and Analgesia* 1981; **60**: 12–17.
5. Mirakhur RK, Pandit SK, Ferres CJ, Gibson FM. Time course of muscle relaxation with a com-

bination of pancuronium and tubocurarine. *Anesthesia and Analgesia* 1984; **63:** 437–40.

6. Mirakhur RK, Ferres CJ, Clarke RSJ, Bali IM, Dundee JW. Clinical evaluation of Org NC 45. *British Journal of Anaesthesia* 1983; **55:** 119–24.
7. Viby-Mogensen J. Clinical assessment of neuromuscular transmission. *British Journal of Anaesthesia* 1982; **54:** 209–23.
8. Ferres CJ, Mirakhur RK, Pandit SK, Clarke RSJ, Gibson FM. Dose–response studies with pancuronium, vecuronium and their combination. *British Journal of Clinical Pharmacology* 1984; **18:** 947–50.
9. Kerr WJ, Baird WLM. Clinical studies on Org NC 45: comparison with pancuronium. *British Journal of Anaesthesia* 1982; **54:** 1159–66.

Anaesthesia, 1986, Volume 41, pages 155–158

Plasma bupivacaine concentrations following psoas compartment block

J. A. ODOOM, W. W. A. ZUURMOND, I. L. SIH, J. BOVILL, G. OSTERLÖF AND H. V. OOSTING

Summary

Fourteen patients undergoing hip replacement surgery under psoas compartment block combined with general anaesthesia were studied. Group 1 ($n = 7$) received plain and Group 2 ($n = 7$) received 0.25% bupivacaine with adrenaline. The mean maximum peak concentrations were 1.93 (SEM 0.46) μg/ml and 1.04 (SEM 0.19) μg/ml at 10 minutes in groups 1 and 2 respectively. Bupivacaine concentrations were higher at all times in the group which received plain than the group receiving solution containing adrenaline. These differences were statistically significant at 10, 15 ($p < 0.05$) and 30 minutes ($p < 0.025$). The highest recorded plasma bupivacaine concentration was 4.54 μg/ml in one patient receiving plain bupivacaine. No patient developed any signs of toxic symptoms. The duration of analgesia was longer ($p < 0.005$) in the group receiving bupivacaine with adrenaline. Bupivacaine 0.25% with adrenaline 1:200 000 is safe for psoas compartment block, and is recommended for hip surgery.

Key words
Anaesthetic techniques, regional; psoas compartment block.
Anaesthetics, local; bupivacaine.

Psoas compartment block may be used to achieve complete analgesia of the lower extremity with minimum side effects. Because of cardiovascular stability,[1] it is preferred to spinal or epidural analgesia, which can cause hypotension.[2] Bupivacaine 0.5% produces profound motor blockade, which can allow subluxation of the joint in the early postoperative period in patients who have undergone hip replacement. Bupivacaine 0.25% produces effective analgesia and motor blockade which is adequate for surgery. However, with this concentration large volumes (30–40 ml) are needed to fill the psoas compartment, in order to ensure complete analgesia. The plasma concentration using this volume has not previously been studied. We therefore measured the plasma concentration of bupivacaine following psoas compartment block using 40 ml 0.25% solution with and without adrenaline 1:200 000.

Methods

Fourteen patients undergoing total hip replacement surgery took part in the study. All gave

---

J.A. Odoom, MD, Staff Anaesthetist, Department of Anaesthesia, W.W.A. Zuurmond, MD, PhD, Acting Head of Department, Department of Anaesthesia, I.L. Sih, MD, Staff Anaesthetist, Department of Anaesthesia, Meibergdreef 9, 1105 AZ, Amsterdam, The Netherlands, J. Bovill, MD, FFARCSI, Professor, Department of Anaesthesia, University Hospital, University of Leiden, Rijnsburgerweg 10, 2333 AA, Leiden, The Netherlands, G. Osterlöf, Technician, Astra Läkemedel AB, Research and Development Laboratories, Bioanalytical Chemistry, Stockholm, Sweden, H.v. Oosting, ir, PhD, Department of Medical Physics, Meibergdreef 9, 1105 AZ, Amsterdam, The Netherlands.
Correspondence to Dr J.A. Odoom please.

0003–2409/86/020155 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

informed consent for the investigation which was approved by the Hospital Ethical Committee. They were randomly allocated to one of two groups. Group 1 ($n = 7$), three males and four females, received 0.25% plain bupivacaine and Group 2 ($n = 7$), four males and three females, received 0.25% bupivacaine with adrenaline (1:200 000). Premedication was with diazepam 10 mg, orally one hour prior to surgery.

On arrival in the operating room, electrocardiogram (ECG) electrodes were applied and an intravenous infusion established. Blood pressure was measured every 5 minutes using an automatic blood pressure monitor. After preoxygenation, anaesthesia was induced with methohexitone, 0.75–1 mg/kg followed by suxamethonium 1 mg/kg to facilitate intubation of the trachea. Anaesthesia was maintained with 60% nitrous oxide and oxygen and 0.4–0.8% enflurane. Patients were allowed to breath spontaneously via a semiclosed circle system, with a gas flow of 6 litres/minute.

Following induction of anaesthesia, a radial artery cannula was inserted percutaneously. The patient was then positioned with the affected side uppermost, and the psoas block performed with the aid of neurotracer (Top Pole, Japan) using the landmarks described by Chayen *et al.*[3] When contraction of the lower limb was observed upon stimulation, an aspiration test was performed to exclude the presence of blood or cerebrospinal fluid (CSF). If this was negative, 40 ml 0.25% bupivacaine either with or without adrenaline was injected. The patient remained in the lateral position for 5 minutes and was then placed in a semilateral position.

Blood sampling

Arterial blood samples (10 ml) for estimation of bupivacaine concentrations were collected into lithium heparin tubes 2, 5, 10, 30, 60, 90, 120, 180 and 240 minutes after the injection of the bupivacaine. The heparinised blood samples were centrifuged and the separated plasma stored at −20° C until analysed.

Bupivacaine measurements

All samples were analysed in duplicate using gas–liquid chromatography as described by Zylber-Katz and colleagues.[4] Duration of analgesia was assessed by timing the intervals between the initial dose of local anaesthetic solution and the administration of postoperative analgesic drugs.

Data were analysed using analysis of variance. Values of $p < 0.05$ were considered significant. Results are expressed as mean (SEM).

Results

The groups were comparable with respect to age, weight, height, blood loss and transfusion requirements (Table 1). The duration of analgesia was longer in the group receiving bupivacaine with adrenaline than the group who received plain bupivacaine ($p < 0.005$).

Bupivacaine concentrations were higher at all times during the 4-hour period in the plain bupivacaine group than in the bupivacaine and adrenaline group. These differences were statistically significant at 10, 15 ($p < 0.05$) and 30 minutes ($p < 0.025$).

The highest peak concentration measured was 4.54 μg/ml following plain bupivacaine and 1.62 μg/ml when adrenaline was included in the solution. These changes occurred at 10 minutes after bupivacaine injection. The time at which peak concentrations occurred varied from 2–15 minutes. The concentrations in individual patients are shown in Tables 2 and 3. The maximum average peak concentrations were 1.94 (SEM 0.46) μg/ml (range: 0.02–4.54) and 1.04 (SEM 0.19) μg/ml (range: 0.07–1.9) in the groups receiving plain and bupivacaine with adrenaline respectively. The average change is shown in

Table 1. Mean (SEM) values of age, weight, height, duration of surgery, duration of analgesia, blood loss and blood transfusion requirements in both groups of patients

Bupivacaine solution	Age (years)	Weight (kg)	Height (cm)	Duration of surgery (minutes)	Duration of analgesia (minutes)	Blood loss (ml) (ml)	Blood transfusion requirements (ml)
No adrenaline	79.1	65.3	160	174	546	1020	750
	(2.3)	(2.4)	(2)	(6)	(60)	(240)	(192.5)
Adrenaline	77.1	68.4	170	180	876*	1060	774
	(3.3)	(3.4)	(2)	(6)	(72)	(120)	(80.5)

*Significant difference between bupivacaine plain and bupivacaine with adrenaline, $p < 0.005$.

Table 2. Mean (SEM) arterial plasma concentrations (μg/ml) of plain bupivacaine in individual patients ($n = 7$)

	Time (minutes										
Patient	0	2	5	10	15	30	60	90	120	180	240
1	0	0.52	1.30	1.80	1.42	1.42	1.05	0.48	0.74	0.62	0.52
2	0	0.92	1.18	0.99	0.79	0.55	0.53	0.76	0.31	0.37	0.71
3	0.02	1.99	1.44	1.29	1.09	0.87	0.68	0.53	0.32	0.16	0.23
4	0	0.24	0.92	4.54	2.33	1.86	1.43	0.45	0.63	0.48	0.42
5	0	0.02	0.67	1.67	1.70	1.01	0.78	1.18	0.61	0.52	0.47
6	0.1	1.72	1.36	1.12	1.01	0.77	0.88	0.78	0.59	0.59	0.56
7	0	1.98	1.10	2.13	4.14	1.94	0.85	0.56	0.64	0.51	0.42
Mean	0	1.06	1.14	1.93	1.78	1.20	0.90	0.68	0.55	0.46	0.48
(SEM)	0	0.32	0.10	0.46	0.44	0.21	0.10	0.10	0.06	0.06	0.06

Table 3. Mean (SEM) arterial plasma concentrations (μg/ml) of bupivacaine with adrenaline (1:200000) in individual patients ($n = 7$)

	Time (minutes)										
Patient	0	2	5	10	15	30	60	90	120	180	240
1	0	0.95	1.09	1.14	0.99	0.85	0.65	0.48	0.49	0.34	0.53
2	0	0.27	1.19	1.38	1.48	1.24	0.89	0.45	0.52	0.52	0.28
3	0.02	1.11	1.06	0.89	0.72	0.49	0.27	0.30	0.29	0.31	0.30
4	0	1.25	1.9	1.50	1.24	0.91	0.78	0.69	0.48	0.28	0.27
5	0	0.96	1.27	1.62	1.20	0.78	0.59	0.55	0.47	0.29	0.40
6	0.03	0.18	0.21	0.43	0.36	0.45	0.33	0.29	0.32	0.50	0.31
7	0	0.07	0.17	0.33	0.43	0.73	0.69	0.55	0.47	0.39	0.54
Mean	0.00	0.68	0.98	1.04	0.92	0.79	0.60	0.47	0.43	0.37	0.38
(SEM)	0.00	0.19	0.23	0.19	0.16	0.10	0.09	0.05	0.03	0.04	0.04

Fig. 1. The highest recorded plasma concentration was 4.54 μg/ml. Two patients, both receiving bupivacaine, had a plasma concentrations above 4 μg/ml (Tables 2 and 3). No patient developed toxic symptoms.

Discussion

The maximum recommended dose of bupivacaine in any 4-hour period is 2 mg/kg.[5] This dose is higher than that used in the present study (1.5 mg/kg).

The average peak arterial concentrations obtained in the group receiving plain bupivacaine was 1.93 μg/ml, and 1.04 μg/ml when adrenaline was used. These levels are comparable to those concentrations reported following epidural and intercostal nerve blocks with bupivacaine.[6] How-

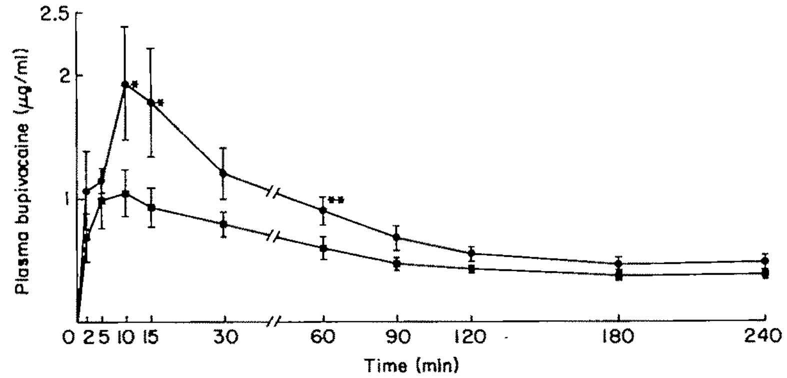


Fig. 1. Arterial plasma concentrations following psoas compartment block using 0.25% bupivacaine. Mean values (SEM). Asterisks indicate level of significance between plain and bupivacaine with adrenaline: *$p < 0.05$; **, $p < 0.025$. (●——●), plain bupivacaine; (■——■), bupivacaine with 1:200000 adrenaline.

ever, in two of the patients receiving plain 0.25%, the plasma concentrations measured were 4.54 μg/ml and 4.14 μg/ml, which are above the reported toxic plasma bupivacaine concentrations (2–4 μg/ml) in man.[7,8] None of the patients in this study developed systemic toxicity, and this is probably due to the concomitant use of diazepam premedication and general anaesthesia, both of which suppress toxic effects.[9,10]

The average plasma concentrations of bupivacaine in this study were statistically higher at 10, 15 ($p < 0.05$), and 30 minutes ($p < 0.025$) in those patients who received the plain solution than in those who received bupivacaine with adrenaline.[11–13] However, there was a large variability of peak plasma concentrations in individual patients (Tables 2 and 3). Our findings are consistent with the report of Neill and Watson,[5] who found significantly higher peak concentrations in patients receiving 0.5% plain bupivacaine than in those receiving bupivacaine with adrenaline for fifth cranial nerve and cervical plexus blocks.

In this study, addition of adrenaline to bupivacaine was effective in prolonging the analgesic duration. Similar findings have been previously reported.[14] Colley *et al.*,[15] however, found no difference in either the plasma concentrations or the duration of analgesia in patients receiving 0.25% bupivacaine with and without adrenaline (1:200 000) for scalp infiltration. The difference between the findings of these authors and the results presented in this study might have been due to the different site of injection of the local anaestheic.[11,12] It has also been reported that the effect of adrenaline on duration of analgesia depends on both the local analgesic agent used and the type of regional procedure performed.[16]

In conclusion, this study has demonstrated that the use of 40 ml 0.25% bupivacaine containing adrenaline (1:200 000) for psoas compartment block is safe, and it is recommended for hip surgery.

Acknowledgments

The authors thank the staff of the Orthopaedic Department for their cooperation, and Dr P. Brasem of Astra Pharmaceutica, The Netherlands, for his excellent assistance. This work was partly supported by Astra Läkemedel AB, Stockholm, Sweden.

References

1. WHITE IWC, CHAPPELL WA. Anaesthesia for surgical correction of fractured femoral neck. A comparison of three techniques. *Anaesthesia* 1980; **35:** 1107–10.
2. DAGNINO J, PRYS-ROBERTS C. Studies of anaesthesia in relation to hypertension. VI: Cardiovascular responses to extradural blockade of treated and untreated hypertensive patients. *British Journal of Anaesthesia* 1984; **56:** 1065–73.
3. CHAYEN D, NATHAN H, CHAYEN M. The psoas compartment block. *Anesthesiology* 1976; **45:** 95–9.
4. ZYLBER-KATZ E, GRANIT L, LEVY M. Gas–liquid chromatographic determination of bupivacaine and lidocaine in plasma. *Clinical Chemistry* 1978; **24:** 1573–5.
5. NEILL RS, WATSON R. Plasma bupivacaine concentrations during combined regional and general anaesthesia for resection and reconstruction of head and neck carcinomata. *British Journal of Anaesthesia* 1984; **56:** 485–92.
6. MOORE DC, MATHER LE, BRIDENBAUGH PO, BRIDENBAUGH LD, BALFOUR RI, LYSONS DF, HORTON WG. Arterial and venous plasma levels of bupivacaine following epidural and intercostal nerve bocks. *Anesthesiology* 1976; **45:** 39–45.
7. JORFELDT L, LOFSTROM B, PERNOW B, PERSSON B, WAHREN J, WIDMAN B. The effect of local anaesthetics on the central circulation and respiration in man and dog. *Acta Anaesthesiologica Scandinavica* 1968; **12:** 153–69.
8. TUCKER GT, MATHER LE. Clinical pharmacokinetics of local anaesthetics. *Clinical Pharmacokinetics* 1979; **4:** 241–78.
9. MOORE DC, BALFOUR RI, FITZGIBBONS D. Convulsive arterial plasma levels of bupivacaine and the response to diazepam therapy. *Anesthesiology* 1979; **50:** 454–6.
10. JONG RH DE, HEAVNER JE DE, OLIVEIRA LF. Effects of nitrous oxide on the lidocaine seizure threshold and diazepam protection. *Anesthesiology* 1972; **37:** 299–303.
11. HOLLMEN A, OJALA A, KORHONEN M. Paracervical block with marcaine-adrenaline. *Acta Anaesthesiologica Scandinavica* 1969; **13:** 1–9.
12. WILKINSON GR, LUND PC. Bupivacaine levels in plasma and cerebrospinal fluid following peridural administration. *Anesthesiology* 1970; **33:** 482–6.
13. REYNOLDS F, TAYLOR G. Plasma concentrations of bupivacaine during continuous epidural analgesia in labour: the effect of adrenaline. *British Journal of Anaesthesia* 1971; **43:** 436–40.
14. SINCLAIR CJ, SCOTT DB. Comparison of bupivacaine and etidocaine in extradural blockade. *British Journal of Anaesthesia* 1984; **56:** 147–53.
15. COLLEY PS, HAEVNER JE. Blood levels of bupivacaine after injection into the scalp with and without epinephrine. *Anesthesiology* 1981; **54:** 81–4.
16. COVINO BG, BUSH DF. Clinical evaluation of local anaesthetic agents. *British Journal of Anaesthesia* 1975; **47:** 289–96.

Anaesthesia, 1986, Volume 41, pages 159–161

Pretreatment with opioids

The effect on thiopentone induction requirements and on the onset of action of midazolam

J. W. DUNDEE, N. J. HALLIDAY, T. J. McMURRAY AND K. W. HARPER

Summary

Pretreatment with small doses of fentanyl (100 μg) or alfentanil (300 μg) was found significantly to reduce the induction dose of thiopentone. Fentanyl 50 μg and alfentanil 150 μg also significantly reduced the onset time and increased the consistency of action of midazolam. Respiratory depression was not a problem when 50 μg fentanyl or 150 μg alfentanil were used.

Key words

Anaesthetics, intravenous; thiopentone, midazolam.
Analgesics, narcotic; fentanyl, alfentanil.

The delayed and variable action of midazolam in inducing anaesthesia has been outlined in previous studies.[1] Used alone, we found midazolam to be unsuitable for the induction of anaesthesia in younger patients. By contrast, thiopentone is a reliable and rapidly acting induction agent and, if it were not for accompanying cardiovascular and respiratory depression, would be the ideal induction agent.

Various premedicant drugs, including intramuscular morphine with hyoscine, have been shown to decrease the requirements of thiopentone.[2] However, intramuscular opiate premedication is less than ideal;[3] it involves administrative problems for nursing staff in recording the use of a controlled drug and in giving an injection. Furthermore, it may cause nausea, respiratory depression and, less commonly, hypotension. Oral premedication with a benzodiazepine has become increasingly popular, but oral diazepam improves neither the reliability nor the rapidity of induction of intravenous midazolam.[4]

Although not providing pre-operative anxiolysis, intravenous pretreatment in the operating theatre with a short-acting opioid such as fentanyl or alfentanil offers an alternative to the intramuscular use of morphine or pethidine. Here, we report the effect of such pretreatment on the induction dose of thiopentone and the speed of onset and reliability of intravenous midazolam. It was not possible to measure directly the 'induction dose' of a slowly acting drug such as midazolam, the clinically important feature being the onset time in those patients who lose consciousness within 2–3 minutes.

Method

Studies were carried out on fit, unpremedicated patients scheduled for operations for which either thiopentone or midazolam could be the induction agent of choice. Their ages ranged from 16–50 years. There were five groups induced with midazolam and three with thiopentone, one of which

---

J.W. Dundee, MD, PhD, FRCP, FFARCS, Professor, N.J. Halliday, MB, FFARCS, Senior Tutor, T.J. McMurray, MD, FFARCS, Senior Tutor, K.W. Harper, MB, FFARCS, Senior Tutor, Department of Anaesthetics, The Queen's University of Belfast, Northern Ireland.

0003–2409/86/020159 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

acted as a 'control', with no pretreatment. Thiopentone was preceded by 100 μg fentanyl or an equipotent dose of alfentanil 300 μg intravenously over 2 minutes, with additional groups receiving 50 μg fentanyl or 150 μg alfentanil before midazolam. A further 2 minutes elapsed before induction with thiopentone or midazolam was commenced. The pretreatments were allocated in random order in both the thiopentone and midazolam series but both were run concurrently with other similar studies and this explains the difference in patient numbers in the various series in Tables 1 and 2.

The dose of thiopentone was estimated using the method described by Dundee *et al.*[2] An initial dose of 2 mg/kg of 2.5% solution was given into a large antecubital vein over 10 seconds; after a further 30 seconds, the eyelash reflex was tested and increments of 25 mg were given every 15 seconds until this was abolished. The induction dose of midazolam was standardised at 0.3 mg/kg and was injected into a large antecubital vein over 20 seconds. The induction time was taken from the end of injection until verbal contact with the patient was lost. If this had not occurred by 3 minutes, the induction time was noted as 180 + seconds and anaesthesia was completed with inhalational agents.

In view of the sex difference in the induction dose of thiopentone,[2,5] the thiopentone studies were all carried out on women. This sex difference has not been demonstrated with midazolam;[5] studies were therefore carried out in patients of both sexes.

Results

Table 1 shows that the numbers and physical characteristics of the patients in the three groups who received thiopentone were broadly comparable. Also expressed here are the mean thiopentone requirements in mg/kg and, in view of the non-linearity of the distribution, also in $\log_e$ mg/kg. It can be seen that pretreatment with both fentanyl and alfentanil significantly decreases the 'induction' dose of thiopentone ($p < 0.001$ when expressed in both mg/kg and $\log_e$ mg/kg).

Table 1. Anthropomorphic data, mean and mean $\log_e$ thiopentone requirements in control and fentanyl or alfentanil pretreated groups

	n	Mean age (years, SEM)	Mean weight (kg, SEM)	Mean dose (mg/kg, SEM)	Mean $\log_e$ dose (mg/kg, SEM)
Control	39	41 (2.1)	60 (1.8)	4.60 (0.17)	1.51 (0.04)
Fentanyl 100 μg	51	38 (1.8)	62 (1.8)	3.30 (0.16)	1.16 (0.04)
Alfentanil 300 μg	37	37 (1.8)	63 (2.5)	3.76 (0.17)	1.40 (0.05)

Table 2. Anthropomorphic data, mean induction times and % of patients asleep by 3 minutes, following intravenous midazolam 0.3 mg/kg in fentanyl, alfentanil and unpretreated groups

		n	Mean age (years, SEM)	Mean weight (kg, SEM)	Mean induction time (seconds, SEM)	Mean $\log_e$ induction time (seconds, SEM)	% asleep at 3 minutes
Control		110	38 (3.3)	62 (0.1)	113.7 (1.07)	4.53 (0.06)	60
Fentanyl	50 μg	52	32 (1.2)	62 (1.6)	77.9 (7.08)	4.13 (0.07)	85
	100 μg	52	34 (1.1)	65 (1.7)	58.2 (5.71)	3.91 (0.07)	92
Alfentanil	150 μg	40	33 (1.1)	63 (1.6)	76.4 (5.16)	4.13 (0.07)	85
	300 μg	40	34 (1.1)	60 (1.3)	55.9 (5.48)	3.95 (0.08)	90

Table 2 gives the relevant findings for midazolam. Whether the mean induction time is expressed as in absolute time or as the mean of the log time, there is a highly significant reduction in both fentanyl and alfentanil pretreated groups ($p < 0.001$). Furthermore, potentiation by opioid pretreatment can be seen, with a significantly greater number of patients asleep by 3 minutes ($p < 0.001$).

In the doses used, both fentanyl and alfentanil produced a similar reduction in thiopentone induction dosage. This also applied to the onset time with midazolam. The difference between the action of the doses of the two opioids is not significant with respect to onset time or frequency of induction of anaesthesia; apnoea did not occur with the lower dose of either opioid, while assisted ventilation was occasionally required when midazolam was given after 100 μg fentanyl or 300 μg alfentanil.

Discussion

The reduction in thiopentone requirements following pretreatment with these small doses of fentanyl and alfentanil would be advantageous in frail or elderly patients, whose cardiovascular status may be impaired. Furthermore, the inclusion of a potent intravenous analgesic agent will be important in certain painful operations, bearing in mind that thiopentone has no analgesic action of its own. This is not likely to be a pharmacokinetic potention, but rather the action of two different types of drugs (hypnotic and analgesic) contributing to the clinical state of anaesthesia.

There is greater reliability and more rapid onset of sleep following opioid pretreatment and midazolam induction in the hitherto resistant younger age group. The benzodiazepine–opioid combination is associated with cardiovascular stability and is used to induce anaesthesia for cardiac surgery.[6] Apnoea or clinical respiratory depression was not a feature in any patient receiving the lower doses of either opioid, which would seem adequate to potentiate the benzodiazepine. Although specifically studied, one would not expect the shorter-acting alfentanil to be associated with a more rapid recovery than equivalent doses of fentanyl.

References

1. Dundee JW, Halliday NJ, Loughran PG, Harper KW. Some factors influencing the response to midazolam. *British Journal of Anaesthesia* 1984; **56:** 804–5P.
2. Dundee JW, Hassard TH, McGowan WAW, Henshaw J. The 'induction' dose of thiopentone. *Anaesthesia* 1982; **37:** 1176–84.
3. Dundee JW, Loan WB, Clarke RSJ. Studies of drugs given before anaesthesia. XI: Diamorphine (heroin) and morphine. *British Journal of Anaesthesia* 1966; **38:** 610–9.
4. Gamble JAS, Kawar P, Dundee JW, Moore J, Briggs LP. Evaluation of midazolam as an intravenous induction agent. *Anaesthesia* 1981; **36:** 868–73.
5. Dundee JW, Halliday NJ, Loughran PG. Age and sex as factors influencing the onset of action of intravenous midazolam. *Irish Journal of Medical Science* 1984; **152:** 225–6.
6. Kawar P, Carson IW, Lyons SM, Clarke RSJ, Dundee JW. Haemodynamic changes during induction of anaesthesia with midazolam and diazepam (Valium) in patients undergoing aorto-coronary bypass surgery. *British Journal of Anaesthesia* 1983; **55:** 915–6P.
7. Patrick M, Eagar BM, Toft DF, Sebel PS. Alfentanil-supplemented anaesthesia for short procedures. A double-blind comparison with fentanyl. *British Journal of Anaesthesia* 1984; **56:** 861–6.

Anaesthesia, 1986, Volume 41, pages 162–167

The haemodynamic effects of bronchoscopy

Effect of pretreatment with fentanyl and alfentanil

KATHERYN J. WARK, J. LYONS AND R. O. FENECK

Summary

The cardiovascular responses to bronchoscopy under general anaesthesia were investigated in 36 premedicated patients. Twelve patients acting as controls received a standard intravenous anaesthetic of intermittent thiopentone and suxamethonium. A further 24 patients were given either fentanyl 6 μg/kg or alfentanil 18 μg/kg intravenously, one minute prior to induction. There were significant rises in systolic arterial blood pressure ($p < 0.05$) and in rate pressure product ($p < 0.05$) in the patients in the control group, but these changes were not seen in those patients receiving either fentanyl or alfentanil. However, dysrhythmias and ST segment changes indicative of myocardial ischaemia were present in some patients in all three groups.

Key words

Anaesthetic techniques; bronchoscopy.
Analgesics, narcotic; fentanyl, alfentanil.

The haemodynamic effects of laryngoscopy and intubation have been shown to be due to a sympatho-adrenal response to stimulation of the upper respiratory tract.[1] Laryngoscopy produces a marked rise in heart rate and in arterial blood pressure.[2,3] Bronchoscopy entails more manipulation of the upper and lower respiratory tracts takes a significantly longer time, and would be expected to produce a longer and possibly more severe hypertensive response.

These pressor responses are of short duration and are usually well tolerated. However, untoward effects may occur, in particular dysrhythmias and a rise in myocardial oxygen consumption. Myocardial ischaemia may result,[4,5] and may be especially worrying in those patients with pre-existing hypertension and ischaemic heart disease, and in the elderly with accompanying lung disease. Such patients are frequently amongst those who present for bronchoscopy, which itself is predictably even more stressful than laryngoscopy in its effects on the cardiovascular system[6–8] and therefore represents a potentially greater hazard to safe anaesthesia.

There have been many attempts to attenuate these adverse effects. They include topical anaesthesia[9] and systemic lignocaine,[10] both of which only partially suppress the response. Alpha[11] and beta blockers,[12] nitroprusside[13] and hydralazine[14] have also been tried. Many of these have adverse and long lasting effects, and the use of some of these agents may require invasive monitoring, which is not always appropriate to

---

K.J. Wark, FFARCS, Senior Registrar, Anaesthetic Department, The London Hospital, Whitechapel, London E1, J. Lyons, MRCP, Lecturer in Cardiology, Cardiac Department, R.O. Feneck, FFARCS, Consultant, Anaesthetic Department, London Chest Hospital, Bethnal Green, London E2.

0003–2409/86/020162 + 06 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

the patient's physical status and scheduled operation. Midazolam[15] and deeper inhalational techniques[16] have both been recommended, but show a variable response. Routine premedication also does not obtund this response.[2] Fentanyl, in a dose of 2 μg/kg in combination with thiopentone has been shown to attenuate the arterial pressure and heart rate increases produced by laryngoscopy and intubation,[16–18] while a dose of 6 μg/kg completely abolishes it.[17] We therefore decided to study its effectiveness during bronchoscopy, together with alfentanil which has one third of the potency of fentanyl.[19]

Methods

Thirty-six patients presenting for bronchoscopy followed by another procedure were studied following local Ethical Committee approval. They were randomly allocated to either the control, fentanyl or alfentanil group. All patients were physical status ASA groups 1–3. They were examined pre-operatively by an anaesthetist, and written consent was obtained after the procedure had been fully explained to them.

Prior to premedication, a battery-powered, continuous ECG cassette recorder was attached to the patient using leads in the CM5 and reverse CM5 positions. Premedication was with pethidine 1–1.5 mg/kg, promethazine 25 mg and atropine 0.6 mg intramuscularly, one hour pre-operatively. On arrival in the anaesthetic room, the patient was connected to a non-invasive automated oscillometric blood pressure monitoring device (Datascope Accutorr), which monitored the blood pressure at one-minute intervals. Groups 2 and 3 received fentanyl 6 μg/kg or alfentanil 18 μg/kg through an indwelling intravenous cannula. One minute later, all three groups received thiopentone to obtund the eyelash reflex, followed by suxamethonium 1 mg/kg. The patients' lungs were ventilated via a facemask with 100% oxygen and, following full muscular relaxation, laryngoscopy was performed and the larynx sprayed with 4 ml 4% lignocaine.

Bronchoscopy was performed and the patients' lungs were ventilated using the Sander's injector technique with 100% oxygen. Incremental doses of thiopentone or suxamethonium were given as required, but not less than 50 mg thiopentone every 2 minutes or 25 mg suxamethonium every 5 minutes. An arterial blood gas sample was taken at the end of the procedure. The ECG cassette tape was later analysed for rhythm and rate changes or S-T depression using an Oxford Medilog Analyser. The data were analysed using paired and unpaired Student's *t*-test for the first 7 minutes of the study.

Results

The pre-induction patient data are shown in Table 1. There was no significant difference between the groups. The time taken for the procedure and the dosages of drugs used is listed in Table 2. The changes in pulse rate are shown in Table 3. There was a significant rise ($p < 0.05$) in the pulse rate in the control group at one and 2 minutes after the commencement of the bronchoscopy when compared to pre-induction values. There was a significant difference ($p < 0.05$) between the pulses recorded at the post-laryngoscopy and one minute after commencement of bronchoscopy between the control group and the fentanyl group. There was a significant difference ($p < 0.05$) between the alfentanil and the control group at the post-laryngoscopy recording and up to 3 minutes after the commencement of bronchoscopy.

Table 4 shows the changes in arterial blood pressure. There was a significant rise ($p < 0.05$) in the control group following laryngoscopy and the commencement of bronchoscopy which lasted for 5 minutes. This is also reflected in the mean and diastolic values. There was a significant fall ($p < 0.05$) in the pressure in the fentanyl and

Table 1. Mean (SEM) values of pre-induction patient data in the different groups

Group	Age (years)	Sex	Weight (kg)	MAP (mmHg)	Pulse (bpm)	RPP (bpm mmHg)
1	53	8 M	69.5	108	93	12685
	(3.6)	4 F	(3.7)	(3.5)	(4.1)	(831)
2	57	9 M	69.5	109	94	13353
	(3.5)	3 F	(3.5)	(3.1)	(5.8)	(1115)
3	60	8 M	68.5	102	86	11328
	(3.3)	4 F	(3.5)	(3.1)	(4.7)	(767)

No significant difference between groups (unpaired *t*-tests).

Table 2. Dosage of drugs used, mg/kg/minute (SEM)

Group	Time (minutes)	Thiopentone total dose (mg)	Thiopentone (mg/kg/minute)	Suxamethonium total dose (mg)	Suxamethonium (mg/kg/minute)
1	7.6	633	1.3	122	0.25
	(0.6)	(38.2)	(0.1)	(7.6)	(1.01)
2	8.1	460	1.1	115	0.25
	(1.2)	(38.7)	(0.2)	(9.5)	(0.03)
3	7.2	483	1.3	116	0.33
	(1.0)	(37)	(0.2)	(8.1)	(0.06)

No significant difference between groups.

Table 3. Mean pulse changes, beats/minute (SEM)

				Post-bronchoscopy						
Group	Pre-induction	Post-induction	Post-laryngoscopy	1 Minute	2 Minute	3 Minute	4 Minute	5 Minute	6 Minute	7 Minute
Control	93	95	99	108*	112*	105	105	102	107	101
	(4.1)	(4.4)	(5.9)	(5.8)	(9.1)	(5.3)	(6.6)	(5.6)	(7.4)	(5.2)
Fentanyl	94	91	91†	89†	88	89	89	86	87	88
	(5.8)	(5.5)	(5.7)	(5.4)	(5.1)	(5.8)	(5.1)	(5.4)	(4.8)	(4.6)
Alfentanil	86	88	88†	89†	87†	87†	86	90	92	93
	(4.7)	(4.2)	(5.2)	(3.9)	(4.4)	(4.0)	(4.4)	(4.5)	(3.2)	(2.3)

*Significant rise ($p<0.05$) compared to pre-induction values.
†Significant difference ($p<0.05$) compared to control group values.

alfentanil groups at the post-laryngoscopy recording. There was a significant difference ($p<0.05$) between the control group and the fentanyl group from the post-laryngoscopy recording until 5 minutes after the commencement of the bronchoscopy. The alfentanil group was also significantly different ($p<0.05$) from the control group according to the post-laryngoscopy recording, until 4 minutes following the commencement of bronchoscopy.

Table 4. Blood pressure changes, mmHg (SEM)

					Post-bronchoscopy						
Group		Pre-induction	Post-induction	Post-laryngoscopy	1 Minute	2 Minute	3 Minute	4 Minute	5 Minute	6 Minute	7 Minute
Control	S	136	132	151*	171*	167*	163*	157*	157	146	140
		(4.1)	(3.7)	(9.3)	(9.3)	(8.9)	(7.1)	(6.7)	(8.1)	(5.5)	(5.0)
	D	83	84.5	100	101	114	111	108	108	105	97
		(3.5)	(2.2)	(6.9)	(6.7)	(6.2)	(6.2)	(5.0)	(6.4)	(4.7)	(2.7)
	M	108	102	119	137*	134*	126*	124*	124*	112	112
		(3.5)	(2.7)	(8.6)	(8.3)	(7.6)	(7.6)	(5.0)	(5.8)	(3.8)	(3.6)
Fentanyl	S	137	134	112†‡	126‡	134‡	133‡	130‡	126‡	128	124
		(4.6)	(4.4)	(5.1)	(5.5)	(8.2)	(8.4)	(8.8)	(5.8)	(7.5)	(8.0)
	D	84	82	70‡	81‡	85‡	84‡	81‡	81‡	84	70
		(2.7)	(2.9)	(4.6)	(4.4)	(5.4)	(5.2)	(5.9)	(4.4)	(5.2)	(4.5)
	M	109	99†	87†‡	98‡	104‡	102‡	102‡	101‡	102	98
		(3.1)	(4.0)	(5.4)	(5.5)	(6.9)	(6.6)	(7.2)	(8.0)	(8.2)	(6.0)
Alfentanil	S	131	123	113†‡	130‡	139‡	134‡	130‡	133	135	125
		(3.3)	(4.2)	(6.3)	(6.2)	(7.2)	(7.8)	(8.7)	(8.7)	(8.6)	(6.7)
	D	82	76	70‡	83‡	88‡	87†	85‡	87‡	82	81
		(2.6)	(3.5)	(5.0)	(4.9)	(5.9)	(5.0)	(6.3)	(7.4)	(5.3)	(6.0)
	M	101	95	86†‡	99‡	107‡	105‡	105‡	103‡	102	96
		(3.1)	(4.0)	(5.4)	(5.5)	(6.9)	(6.6)	(7.2)	(7.9)	(8.2)	(5.9)

*Significant rise ($p<0.05$) compared to pre-induction values.
†Significant fall ($p<0.05$) compared to pre-induction values.
‡Significant difference ($p<0.05$) compared to control values.
S = systolic; D = diastolic; M = mean.

Table 5. Rate pressure product change, beats/minute/mmHg (SEM)

Group	Pre-induction	Post-induction	Post-laryngoscopy	Post-bronchoscopy 1 Minute	2 Minute	3 Minute	4 Minute	5 Minute	6 Minute	7 Minute
Control	12685	12758	15183	18101*	19651*	17830*	16759*	16493*	15978*	14790*
	(831)	(727)	(1629)	(1666)	(1805)	(1394)	(1039)	(1227)	(1314)	(1045)
Fentanyl	13353	12574	10193†‡	11175‡	12907‡	11588‡	11257‡	11011‡	11054‡	10544‡
	(1115)	(1011)	(993)	(1085)	(1225)	(1163)	(1172)	(880)	(1077)	(1097)
Alfentanil	11328	10613‡	10012‡	11674‡	12088‡	11973‡	11528‡	12263‡	12346	11538
	(767)	(552)	(1020)	(951)	(987)	(1044)	(1126)	(1209)	(1190)	(856)

*Significant rise ($p<0.05$) from pre-induction values.
†Significant fall ($p<0.05$) from pre-induction values.
‡Significant difference ($p<0.05$) from control values.

The rate pressure product as shown in Table 5 showed a significant rise ($p<0.05$) in the control group from one to 5 minutes following the commencement of bronchoscopy. In both the alfentanil and the fentanyl groups, there was a significant drop ($p<0.05$) at the post-laryngoscopy measurement, but there were no significant differences in the other recordings when compared to pre-induction values. There were no other significant changes in the alfentanil group.

Significant S-T depression, that is greater than 1 mm, occurred in four patients in the control group, one in the fentanyl group and two in the alfentanil group. One of the patients in the alfentanil group had S-T depression associated with the onset of atrial fibrillation. He had not been previously digitalised. A patient in the control group developed multiple nodal and ventricular ectopics following the S-T changes, and one patient developed S-T segment changes associated with an increase in the rate of pre-existing atrial fibrillation. He had not been previously digitalised. One of the alfentanil group had bigeminy, not associated with significant S-T changes, and several of the patients in all groups had occasional ventricular ectopics.

The blood gases recorded at the end of the procedure are recorded in Table 6. As can be seen, all the patients were well oxygenated and $P\text{aCO}_2$ values were well controlled. We do not consider that the blood gas values in any way affected our readings.

Discussion

This study has shown that bronchoscopy produces a significant rise in blood pressure but little alteration in pulse rate, and a significant rise in the rate pressure product (RPP). This rise in the latter, which is persistent, may be of some concern, particularly as the threshold for ischaemia varies from 18 000 to 40 000 with a mean of about 26 000,[20-22] although there is some question about the significance of this.[23]

In this study, the use of fentanyl 6 μg/kg or alfentanil 18 μg/kg has successfully obtunded this response. Unfortunately, this technique would produce significant postoperative respiratory depression if used for bronchoscopy alone. Therefore, it is only useful when bronchoscopy is followed by another procedure. Interestingly, we did not record a significant rise in pulse rate in the control or the study groups at laryngoscopy, unlike the study by Black, Kay and Healy,[24] and such a rise was only recorded for a short period during the bronchoscopy. We are convinced that none of our patients was awake and administered a sufficient repeated bolus dose of thiopentone in the presence of narcotic premedication to ensure this. There was no incidence of awareness.

Table 6. Blood gases at end of procedure $F\text{IO}_2$, 1.0; kPa (SEM)

	Thiopentone group	Fentanyl group	Alfentanil group
$P\text{aCO}_2$	4.6	5.4	5.24
	(0.62)	(0.69)	(0.21)
$P\text{aO}_2$	20.5	20.6	22.5
	(3.43)	(3.34)	(2.61)

The accuracy and hence usefulness of indirect indicators of myocardial oxygen consumption are currently of much interest in anaesthesia. An attempt was made to correlate rate pressure product with S-T changes, but none could be found and although there were more patients with significant S-T depression in the control group, there were other patients in the study groups who had S-T changes in spite of a lower RPP change. We are not sure of the significance of the S-T changes that were seen. One millimetre depression of the S-T segment during a stressful manoeuvre such as an exercise test is a good indicator of ischaemic heart disease in patients with other risk factors, i.e. middle aged/elderly males, smokers, etc.[25] Nevertheless, in any study there is an incidence of false positive results, usually distributed amongst the low risk group, such as young, female, non-smokers, etc.[26] By the nature of their lung disease and their high age distribution, it would appear that the patients in this study tended more towards the higher risk group and the ECG changes seen in them are therefore of concern, and would warrant further investigation. The Datascope Accutor for blood pressure recordings was used throughout, and we have previously shown that it is accurate in the range that we were using and correlates well with direct measurements of arterial blood pressure.

This study has shown that there is a significant rise in systolic blood pressure and rate pressure product during bronchoscopy using a routine general anaesthetic technique and this may be associated with signs of developing myocardial ischaemia. Fentanyl and alfentanil pretreatment in the doses described did obtund this response in the rate pressure product but we were not able to show a significant decrease in the incidence of myocardial ischaemia as observed by S-T segment changes. Unfortunately, the dosages required of these drugs would significantly depress ventilation for a short procedure such as bronchoscopy alone.

Acknowledgments

The authors would like to thank the surgeons at The London Chest Hospital for their cooperation, and Mrs Amanda Plumer for her secretarial assistance.

References

1. Tomori Z, Widdicombe JG. Muscular, bronchomotor and cardiovascular reflexes elicited by mechanical stimulation of the respiratory tract. *Journal of Physiology* 1969; **200:** 25–49.
2. Millar-Forbes A, Dally FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. *British Journal of Anaesthesia* 1970; **42:** 618–25.
3. King BD, Harris LC Jr, Greifenstein FE, Elder JD Jr, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. *Anesthesiology* 1951; **12:** 556–66.
4. Fox EJ, Sklar GS, Hill CH, Villaneva R, King BD. Complications related to the pressor response to endotracheal intubation. *Anesthesiology* 1977; **47:** 524–5.
5. Prys-Roberts C, Greene LT, Meloche R, Foex P. Studies of anaesthesia in relation to hypertension II: haemodynamic consequences of induction and endotracheal intubation. *British Journal of Anaesthesia* 1971; **43:** 531–46.
6. Jenkins AV. Electrocardiographic findings during bronchoscopy. The apnoeic oxygenation technique. *Anaesthesia* 1966; **21:** 449–56.
7. Jenkins DV. Electrocardiographic findings during bronchoscopy. Use of Sanders' ventilating attachment. *Anaesthesia* 1976; **31:** 548–55.
8. Katz AS, Michelson EL, Stawicki J, Holford FD. Cardiac arrhythmias: frequency during fiberoptic bronchoscopy and correlation with hypoxemia. *Archives of Internal Medicine* 1981; **141:** 603–6.
9. Stoelting RK, Peterson C. Circulatory changes during anaesthetic induction: impact of d-tubocurarine pretreatment thiamylal succinylcholine, laryngoscopy and tracheal lidocaine. *Anesthesia and Analgesia* 1976; **55:** 77–81.
10. Abou-Madi M, Keszler H, Yacoub O. A method for prevention of cardiovascular reactions to laryngoscopy and intubation. *Canadian Anaesthetists Society Journal* 1975; **22:** 316–29.
11. DeVault M, Griefenstein FE, Harris LC. Circulatory responses to endotracheal intubation in light general anesthesia—the effect of atropine and phentolamine. *Anesthesiology* 1960; **21:** 360–2.
12. Prys-Roberts C, Meloche R, Foex P. Studies of anaesthesia in relation to hypertension I: Cardiovascular responses of treated and untreated patients. *British Journal of Anaesthesia* 1971; **43:** 122–37.
13. Stoelting RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with sodium nitroprusside. *Anesthesia and Analgesia* 1979; **58:** 116–9.
14. Davies MJ, Cronin KD, Cowie RW. The prevention of hypertension at intubation—a controlled study of intravenous hydralazine on patients undergoing intracranial surgery. *Anaesthesia* 1981; **36:** 147–51.
15. Boralessa H, Senior DF, Whitwam JG. Cardiovascular response to intubation. A comparative study of thiopentone and midazolam. *Anaesthesia* 1983; **38:** 623–7.
16. Kautto UM. Attenuation of the circulatory response to laryngoscopy and intubation by

fentanyl. *Acta Anaesthesiologica Scandinavica* 1982; **26:** 217–21.

17. Martin, DE, Rosenberg H, Aukburg SJ, Bartkowski RR, Edwards IW, Greenhow DE, Klineling PL. Low-dose fentanyl blunts circulatory responses to tracheal intubation. *Anesthesia and Analgesia* 1982; **61:** 680–4.
18. Dahlgren N, Messeter K. Treatment of stress response to laryngoscopy and intubation with fentanyl. *Anaesthesia* 1981; **36:** 1022–6.
19. Brown JH, Pleuvry BJ, Kay B. Respiratory effects of a new opiate analgesic, R39209, in the rabbit: comparison with fentanyl. *British Journal of Anaesthesia* 1980; **52:** 1101–6.
20. Gobel FL, Nordstom RA, Nelson RR, Jorgensen CR, Wang Y. The rate pressure product as an index of myocardial oxygen consumption during exercise in patients with angina pectoris. *Circulation* 1978; **57:** 549–56.
21. Robinson BF. Relation of heart rate and systolic blood pressure to the onset of pain in angina pectoris. *Circulation* 1967; **35:** 1073–83.
22. Moffitt EA, Dhun H, Gray RJ, De Roberts M, Matloff JM, Bussell JA. Rate pressure product correlates poorly with myocardial oxygen consumption during anaesthesia in coronary patients. *Canadian Anaesthetists' Society Journal* 1984; **31:** 5–12.
23. Barash PG, Kopriva CJ. The rate pressure product in clinical anesthesia; boon or bane? *Anesthesia and Analgesia* 1980; **59:** 229–31.
24. Black TE, Kay B, Healy TEJ. Reducing the haemodynamic responses to laryngoscopy and intubation. A comparison of alfentanil with fentanyl. *Anaesthesia* 1984; **39:** 883–7.
25. Epstein SE. Implications of probability analysis on the strategy used for non-invasive detection of coronary artery disease. *American Journal of Cardiology* 1980; **46:** 491–8.
26. Crawford MH, Mendoza CA, O'Rourke RA, White DH, Boucher CA, Gorwit J. Limitations of continuous ambulatory electrocardiogram monitoring for detecting coronary artery disease. *Annals of Internal Medicine* 1978; **89:** 1–5.

Anaesthesia, 1986, Volume 41, pages 168–172

Assisted ventilation and the Servo ventilator in infants

An assessment of three systems used for CPAP/IMV

R. M. BINGHAM, D. J. HATCH AND P. J. HELMS

Summary

A laboratory assessment was made of systems used for Continuous Positive Airway Pressure/Intermittent Mandatory Ventilation (CPAP/IMV) with the Servo 900B and 900C ventilators. Pressure-volume loops recorded during sine wave oscillation using an external CPAP/IMV system were similar to those found during normal respiration. Pressure–volume loops using the systems based on the ventilator's inbuilt trigger mechanism were very different, particularly for the 900B. The results were confirmed by measurements in two infants. The implications of these findings with reference to the weaning of infants from mechanical ventilation are discussed.

Key words

Ventilation; intermittent positive pressure breathing.
Equipment; ventilators.

Continuous positive airway pressure (CPAP) and intermittent mandatory ventilation (IMV) are now widely used in neonatal and paediatric intensive care.

It has been suggested that infants and neonates experience difficulty breathing spontaneously through the CPAP/IMV mode of the Servo 900B ventilator (Elema Scholander, Sweden).[1,2] This has also been our clinical impression, particularly for premature neonates. Peters and Bennett have suggested a modification of the 900B ventilator, designed to overcome this problem.[1] They connected a piece of narrow bore tubing between the patient end of the breathing system and the inspiratory pressure transducer, in an attempt to reduce the negative pressure which the infant is required to produce at the beginning of inspiration. This modification still requires the infant to trigger the ventilator, as does the recently introduced 900C ventilator. Neither the Peters and Bennett modification nor the 900C have been assessed objectively in infants.

We set out to compare the unmodified 900B and 900C ventilators, the Peters and Bennett modification and a CPAP/IMV system which bypasses the trigger mechanism of the ventilator and is similar to that described for use in adults by Lawler and Nunn[3] (Fig. 1).

Methods

In vitro *measurements*

A standard Servo 900B ventilator, low compliance tubing and Bennett cascade humidifier were connected to a sine wave pump, giving a

---

R.M. Bingham, MB, BS, FFARCS, Senior Registrar*, D.J. Hatch, MB, BS, FFARCS, Consultant, P.J. Helms, PhD, MRCP, Senior Lecturer, Departments of Anaesthesia and Respiratory Medicine, Hospital or Sick Children, Great Ormond Street, London WC1N 3JH.

*Present address: Department of Anaesthesia, St. Bartholomew's Hospital, London EC1A 7BE.

0003–2409/86/020168 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

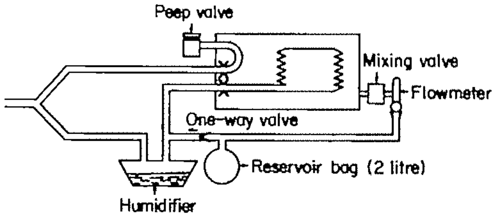


Fig. 1. Diagram of the separate CPAP/IMV system used with the Servo ventilators. During spontaneous ventilation, the ventilator's inspiratory valve is closed and the expiratory valve is open. The patient receives fresh gas at the F_{IO_2} set by the mixing valve, and the level of CPAP is set by the PEEP valve setting. During mandatory breaths, the one-way valve closes and the ventilator functions normally. The continuous fresh gas flow from the flowmeter distends the reservoir bag during inspiration, then vents to atmosphere with the patient's expired gas.

Note: In clinical use, it is advisable to include a pressure relief between the flowmeter and the one-way valve.

tidal volume of 47 ml at a frequency of 40 cycles/minute. The catheter mount joining the pump to the ventilator tubing had two side arms, one of which could be connected to the inspiratory airway pressure transducer of the ventilator by means of a short length of narrow bore, low compliance tubing (after Peters and Bennett). The other side arm was connected with a 23-cm length of low compliance tubing of internal diameter 3 mm to a SE 4-82 pressure transducer (S.E. Laboratories Ltd). A Fleisch type 0 pneumotachograph, attached to a Validyne MP 45 pressure transducer was positioned in the catheter mount. Tidal volumes were electronically integrated from flow. This equipment has been shown to record complete signals at frequencies in excess of 10 Hz,[4] which was more than adequate for this study. Similar measurements were made using the Servo 900C ventilator.

For the unmodified ventilators and the Peters and Bennett modification, the trigger level was set to 0.1 kPa below the CPAP level, in accordance with the manufacturer's instruction manual. With the separate CPAP/IMV system (Fig. 1), the fresh gas flow (FGF) was 6 litres/minute and the ventilator trigger mechanism was not used. The level of CPAP was set using the ventilator's positive end expiratory pressure (PEEP) valve or, in the case of the 900C, the inbuilt PEEP mechanism.

Records of volume and pressure changes were made directly onto sectional graph paper using a fast response XY recorder (Hewlett Packard 7045A). This recorder has a slewing speed of 74 cm/second, and for this study a limit of 10 cm for both axes was adhered to, ensuring that no measurable attenuation would occur at the pump frequencies used. To compute work done during inspiration and expiration, these volume–pressure plots were integrated by tracing their outlines on a digitising table with a resolution of 200 lines per inch (Summagraphics) interfaced with a Prime 750 computer. End expiration was used as a reference point to separate work done by the sine wave pump and the ventilator. Work done by the pump is represented by the areas to the left of the CPAP level during inspiration, and areas to the right of the CPAP level during expiration (Figs 2–4). Work was expressed in Joules/litre of minute ventilation. Pressure and volume changes were recorded for each of the three ventilator systems under test at CPAP levels of 0.5 and 1.0 kPa.

In vivo *measurements*

In order to confirm that the sine wave pump was an appropriate model in the above assessment, volume–pressure plots were obtained using the same apparatus and method in two infants (Figs 3 and 4).

Infant 1 was a three-month-old male, weighing 6 kg, being weaned from mechanical ventilation following surgery for closure of a ventricular septal defect, 24 hours previously. Infant 2 was a five-month-old male weighing 4.4 kg, being weaned from mechanical ventilation 24 hours after a pulmonary valvotomy.

Results

The shape of the volume–pressure plots obtained from the breathing systems based on the ventilator's inbuilt trigger mechanism were very different, both *in vitro* and *in vivo*, from those from the external system. The former were irregular, with marked swings, whilst the latter were elliptical (Figs 2–4).

In the *in vitro* study, the unmodified Servo 900B required a small negative pressure (−0.4 kPa) from the sine wave pump to initiate inspiration. Once the ventilator had cycled to inspiration, gas flow from the ventilator in excess of that required by the pump caused a positive pressure swing and the ventilator's inspiratory valve closed. A further negative pressure swing was

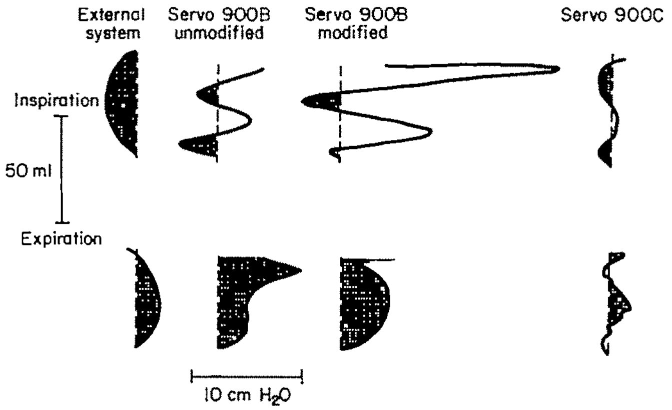


Fig. 2. Pressure volume plots for inspiration and expiration for the different systems *in vitro*. The interrupted line represents the baseline pressures at end expiration. The stippled areas show the work done by the pump in each phase of respiration.

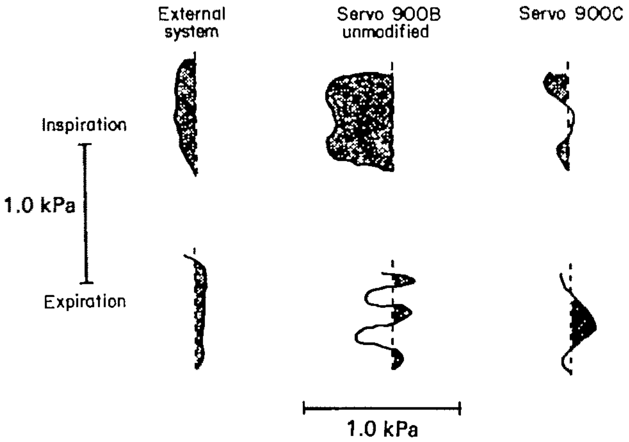


Fig. 3. Pressure-volume plots for inspiration and expiration for the different systems *in vivo*. Infant 1. The interrupted lines represent the baseline pressures at end expiration. The stippled areas show the work done by the pump/infant in each phase of respiration.

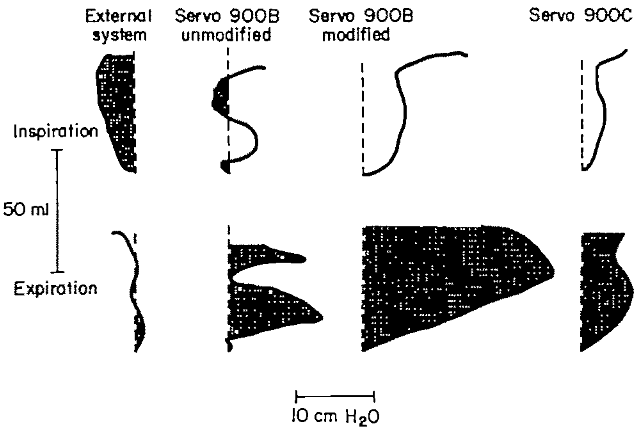


Fig. 4. Pressure volume plots for inspiration and expiration for the different systems *in vivo*. Infant 2. The interrupted lines represent the baseline pressures at end expiration. The stippled areas show the work done by the pump/infant in each phase of respiration.

required from the pump to recycle the ventilator and complete inspiration. A positive pressure from the pump was required to terminate inspiratory flow and initiate expiration; however, once this was achieved, the pressure–volume plot was similar in shape (although larger) to that seen with the external system. The plots seen when the Servo 900C and the Peters Bennett modification of the 900B were used were of a similar shape, although less negative pressure was required to initiate inspiration and, in the case of the Peters and Bennett modification, higher positive pressures were required to terminate inspiratory flow (Fig. 2).

In the *in vivo* studies, the inspiratory waveform obtained with the unmodified Servo 900B was similar to that seen *in vitro*, although the magnitude of the pressure changes and their relationship to the perfect CPAP level varied between patients. In infant 1, gas flow from the 900B ventilator was insufficient to generate a positive pressure at any point during inspiration (Fig. 3). The expiratory pressure swings were larger and more frequent than those seen *in vitro*, and pressure fell well below the CPAP level twice during each expiration. The waveform seen with the Servo 900C in infant 1 was similar to that obtained with the 900B, although much smaller negative pressures were required during inspiration (Fig. 3). No negative pressure was required to initiate inspiration with either the Servo 900C or the Peters and Bennett modification of the Servo 900B in infant 2 (Fig. 4). The pressure remained positive throughout inspiration. High positive pressures occurred during expiration with both these systems in this infant.

Table 1 shows the work done by the sine wave pump and ventilator in the *in vitro* studies. During inspiration, more work is done by the pump when connected to the external system, though during expiration there is little difference between the systems. Total work done by the pump against the extenal system was 3.42×10^{-1} J/litre.

Table 1. Work of breathing requirements in the three CPAP/IMV systems (mJ/litre)

System	Inspiration		Expiration		Total
	Pump	Ventilator	Pump	Ventilator	pump
Unmodified Servo 900B	79	210	150	—	229
Peters and Bennett modification	54	612	161	—	215
Servo 900C	52	28	66	—	118
External system	202	—	140	—	342

All measurements made at 0.5 kPa CPAP.

Discussion

This study was performed to investigate the clinical observation that infants can be weaned more rapidly from mechanical ventilation using the external breathing system described by Lawler and Nunn than with the breathing system built into the Servo ventilator.

Work done by the pump/infant against the external load is represented by the shaded areas in Figs 2–4. Estimation of work is complex in the ventilator based systems. During inspiration, the total work done by the respiratory muscles may be reduced because of work done by the ventilator on the patient's compliance and resistance. In our model, however, it was only possible to measure work in terms of force × distance (pressure × volume). Undetectable isometric work against closed valves will be greater in the two ventilator systems.

The normal work of breathing for a healthy infant at rest is approximately 20–40 m J/litre.[5-9] In the *in vitro* studies, where the sine wave pump was used as a model lung, the additional work imposed by the external breathing system approximately doubled the work of the pump and the ventilator-based systems increased it by between one and two thirds. However, CPAP reduces the work of breathing by about 25%,[10] so it is probable that none of the breathing systems produce unacceptable increases in work. Work of breathing was not calculated in the *in vivo* studies since tidal volume and respiratory rate varied between patients and systems.

Examination of the inspiratory phase of the pressure–volume loops shows that the external system provides a respiratory pattern very similar to normal respiration. The other systems provide very abnormal patterns. This is due to build up of pressure (and/or reduction in flow in the case of the Servo 900C) causing the inspiratory valve to close midway through the inspiratory phase, requiring a further negative pressure from the pump/infant to complete inspiration.

The 'improvement' offered by both the Peters and Bennett modification and the Servo 900C is that the humidifier is no longer between the patient and the pressure transducer. In the case of the 900C, the transducer is on the expiratory limb and in the Peters and Bennett modification the humidifier is bypassed by means of a length of small bore tubing. The result of these modifications is that a smaller negative pressure is required to initiate inspiration. Indeed, with these two systems in infant 2, no negative pressure swing was seen (Fig. 4). This advantage is offset in the Peters and Bennett modification by the larger positive pressure swings required to cycle the ventilator from inspiration to expiration. Cycling from inspiration to expiration required an additional positive pressure in the unmodified Servo 900B. The expiratory limb of the pressure–volume loop was larger (and hence work was greater) in all the ventilator-based systems than with the external system.

In conclusion, it is not possible to explain the clinical observation that infants are more settled on the external system in terms of detectable work of breathing. However, the peaky waveforms seen with the ventilator based systems will involve more hidden work than the elliptical waveform of the external system. It is probable that the unphysiological patterns of inspiration in the ventilator-based breathing systems are unsettling to the infant, and that inflation receptors are abnormally stimulated. This problem is likely to be much more significant with the 900B than the 900C, and this is confirmed in clinical practice. It is possible to wean full term neonates from ventilatory support using the 900C, although some, particularly, if premature, tolerate this breathing less well than the external system.

The near normal pattern of respiration found with the external system, together with the relatively small increase in the work of breathing which it imposes, as opposed to the abnormal patterns seen with all the other systems, provides adequate explanation for its clinical superiority. We suggest it is the preferred system for CPAP/IMV in infants when the Servo 900B and 900C ventilators are used. It is now in routine use in the intensive care units at The Hospital for Sick Children and has proved inexpensive, simple to use and safe.

Acknowledgments

The authors gratefully acknowledge the assistance of Professor W.W. Mapleson DSc, F Inst P. Department of Anaesthetics, University of Wales College of Medicine, Heath Park, Cardiff, CF4 4XN in the preparation of this manuscript.

References

1. Peters CG, Bennett NR. Intermittent assisted ventilation for neonates. *Anaesthesia* 1981; **36:** 806–10.
2. Rendell-Baker L, Feenstra L. The introduction of intermittent mandatory ventilation. *Anaesthesia* 1982; **37:** 473.
3. Lawler PGP, Nunn JF. Intermittent mandatory ventilation. *Anaesthesia* 1977; **32:** 138–47.
4. Beardsmore CS, Helms P, Stocks J, Hatch DJ, Silverman M. Improved oesophageal balloon technique for use in infants. *Journal of Applied Physiology: Respiratory Environmental and Exercise Physiology* 1980; **49:** 735–42.
5. Cook CD, Sutherland JM, Segal S, Cherry RB, Mead J, McIlroy MB, Smith CA. Studies of respiratory physiology in the newborn infant. III. Measurements of mechanics of respiration. *Journal of Clinical Investigation* 1957; **36:** 440–8.
6. Swyer PR, Reiman RC, Wright JJ. Ventilation and ventilatory mechanics in the newborn. *Journal of Pediatrics* 1960; **56:** 612–22.
7. McIlroy MB, Tomlinson ES. The mechanics of breathing in newly born babies. *Thorax* 1955; **10:** 58–61.
8. Krieger I. Studies on mechanics of respiration in infancy. *American Journal of Diseases of Children* 1963; **105:** 439–48.
9. McIlroy MB, Marshall R, Christie RV. The work of breathing in normal subjects. *Clinical Science* 1954; **13:** 127–36.
10. Cogswell JJ, Hatch DJ, Kerr AA, Taylor B. Effects of continuous positive airway pressure on lung mechanics of babies after operation for congenital heart disease. *Archives of Disease in Childhood* 1975; **50:** 799–804.

Anaesthesia, 1986, Volume 41, pages 173–177

Monitoring EEG frequency and amplitude during cardiac surgery

A. MURRAY, A. P. GLARIA AND D. T. PEARSON

Summary

Changes in the electroencephalograms of patients undergoing cardiac surgery with cardiopulmonary bypass were studied. An analysis technique with a simple display of amplitude and frequency within the traditional bands was used. During the course of an operation, there can be dramatic changes in frequency contribution with little or no change in overall EEG amplitude. Evaluation of the results shows that this technique clearly draws attention to periods of EEG change, and examples are given.

Key words

Monitoring; electroencephalography.

Cerebral function monitoring, in one of its many forms, is now accepted as routine practice during cardiac surgery. A number of authors,[1-3] have confirmed the usefulness of the information provided.

A wide variety of electroencephalographic (EEG) monitors are now in clinical use. Many of these are available as standard commercial instruments, but some have been produced by research establishments for their own use. The techniques available include those which analyse the EEG amplitude,[4] EEG spectra,[5] EEG frequency bands,[6] period-amplitude[7] and Hjorth descriptors.[8] It is still relatively common to find only amplitude analysed, with no specific analysis of frequency content other than to tailor the frequency band for amplitude analysis, but it is becoming recognised that frequency and amplitude can vary independently of one another.[6] In addition, there is some evidence that for EEG monitoring during cardiac surgery, many of the techniques which include both amplitude and frequency analyses contain comparable information.[9,10]

We have produced a simple and easy to understand display, which monitors both EEG amplitude and frequency within the normally accepted frequency bands. The work presented here illustrates this new technique with a number of examples obtained during open heart surgery. This paper does not deal with the clinical value of the new technique, but simply with its applicability in an established field of monitoring. It does, however, provide further evidence for the use of a technique which monitors both EEG amplitude and frequency.

Methods

Recording and analysis techniques

The technique in daily use in our open-heart theatres is that using the Cerebral Function

---

A. Murray, PhD, MIEE, CEng, Top Grade Physicist, *A.P. Glaria, MSc, Regional Medical Physics Department, Freeman Hospital, Newcastle upon Tyne, NE7 7DN, D.T. Pearson, FRCP, FFARCS, Consultant Cardiothoracic Anaesthetist, Cardiothoracic Centre, Freeman Hospital, Newcastle upon Tyne, NE7 7DN.

*Present address: Departamento de Fisiologia Normal & Patologica, Universidad de Valparaiso, Valparaiso, Chile, South America.

0003–2409/86/020173 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Monitor (CFM).[4] EEG recordings were taken during surgery by making a connexion between the head pre-amplifier and the main CFM instrument, so as not to interfere in any way with the usual monitoring practice. EEGs were analysed off-line, using a PDP-11 computer and plotted on a Hewlett Packard pen plotter. A Fourier analysis technique was used to obtain the frequency spectrum of the EEG over each 10-second interval, and then the amplitude (rms) of each frequency band was obtained (low delta, upper delta, theta, and alpha). The content of each band was displayed cumulatively, with low delta as the lowest trace and alpha as the uppermost trace. Full details of the techniques used can be obtained from Glaria and Murray.[11]

Problems of artefact were reduced because of the 10-second period over which analysis was carried out. Gross artefact could not be eliminated, but drew attention to itself on the analysis output as sudden and random fluctuations in the spectra.

A semilogarithmic scaling was used when results were plotted. This scale is similar to that of the CFM.[4] Normally, one output point for each frequency band is obtained every 10 seconds, so that fast changes could be observed. However, for clarity of illustration in this report, these results are averaged over 1-minute intervals.

Patients

EEGs from 30 patients were recorded during cardiac surgery using the above techniques. There were 15 children and 15 adults. Five of the recordings could not be analysed because of extensive noise throughout the recording. Five of the children underwent surface hypothermia prior to cardiopulmonary bypass, and, in one of these, surgery was undertaken with total circulatory arrest at a core temperature of 17°C.

The EEG analyses from seven of these patients are represented in this paper, which illustrate the range of results found. Table 1 summarises some of the patient information along with brief details of the EEG analysis results.

Results

Retrospective evaluation of the off-line processed data has shown that there were many instances in which there were profound changes in frequency content with little or no change in amplitude. Figure 1 illustrates this for three children. In all three, there was a sudden increase in low delta frequencies (lowest band) immediately after going on bypass. In Fig. 1a there was an increase in overall amplitude (shown by the upper trace), but in Fig. 1b the amplitude did not change. After a decrease in amplitude, there was a recovery in Fig. 1a and 1c, again with a large content of low delta frequencies compared with before bypass. Figure 1c is particularly interesting in that the overall amplitude is exactly similar before bypass (at 15 minutes) with a period after bypass (at 30 minutes), but both have markedly different frequency distributions.

Figure 2 also illustrates some independence of frequency and amplitude in two adult patients. Here, the changes are less impressive compared with those seen in the children. Both show changes in amplitude after initiation of bypass, but the changes in frequency appear to be more obvious.

In general, the most pronounced changes in the EEG took place immediately after the initiation of cardiopulmonary bypass. An increase in overall EEG amplitude was seen in some patients. Many patients exhibited a large increase in low delta freqencies, with a corresponding reduction in higher frequencies. This was followed in some patients by a reduction in overall EEG amplitude,

Table 1. Summary of patient and EEG analysis information

EEG analysis figure	1a	1b	1c	2a	2b	3	4
Age (y)	5	2	2	62	60	2	54
Weight (kg)	12	14	15	57	76	9	72
Prime (ml)	1600	1400	1600	2000	2500	1600	—
Bypass time (minutes)	63	64	131	71	68	105	77
Minimum temperature (°C)	29	28	23	28	27	17	28
Time to 28°C (minutes)	35*	10	5	17	13	5	25
Minimum voltage (μV)	4	2	2	4	5	1	2
Time to minimum voltage (minutes)	15	5	20	30	35	20	45
Increase in low delta frequency	+	+	+	+		+	+
Fastest changes in low delta	+	+					

*Time to 29°C.

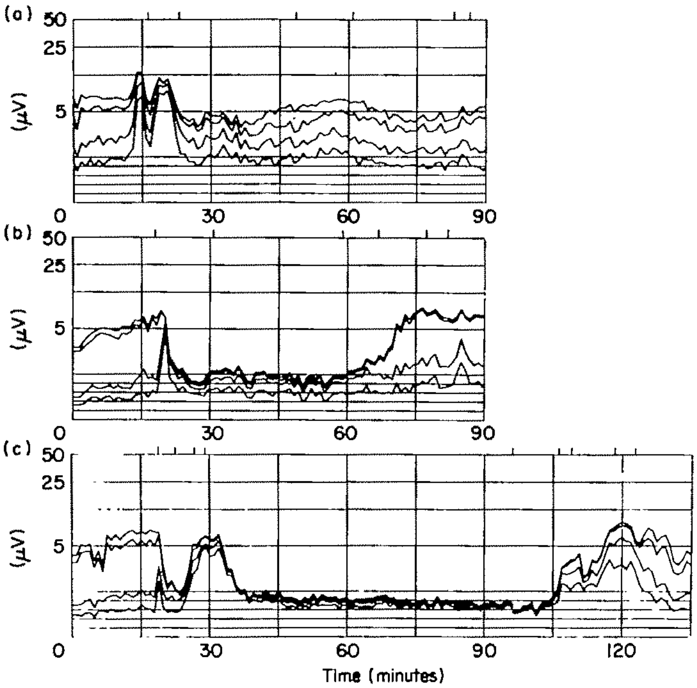


Fig. 1. EEG analysis of three children undergoing open heart surgery. Lowest curve, low delta only; second curve, + upper delta; third curve, + theta; highest curve, + alpha. At the start of bypass there are dramatic changes in the EEG. At times there are periods with little or no changes in amplitude, but with large changes in frequency contribution. Start of bypass—a: 12 minutes, b: 18 minutes, c: 19 minutes. End of bypass—a: 75 minutes, b: 82 minutes, c: 150 minutes (off Fig.).

with a rebound and subsequent fall as the body temperature dropped.

The degree of hypothermia during surgery has a bearing on the EEG amplitude. Temperatures around 28°C produced noticeable falls in EEG amplitude. Two patients with much lower temperatures (23°C and 17°C) produced the lowest EEG levels. The results from the child at 23°C are

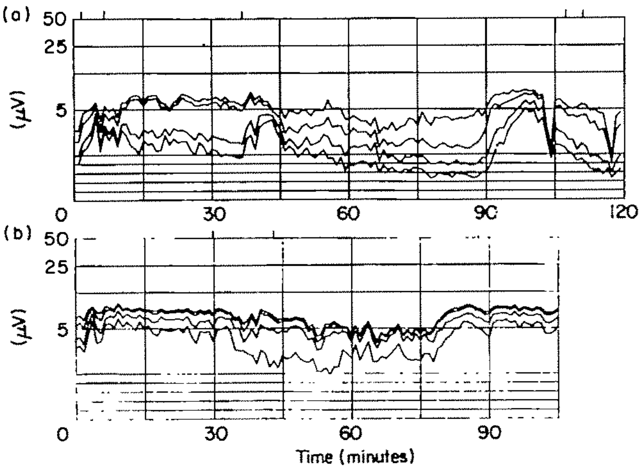


Fig. 2. EEG analysis of two adults undergoing open heart surgery. Initiation of bypass—a: 37 minutes, b: 30 minutes. End of bypass—a: 108 minutes, b: 98 minutes. There are two burst of artefact in A (starting at 102 and 115 minutes).

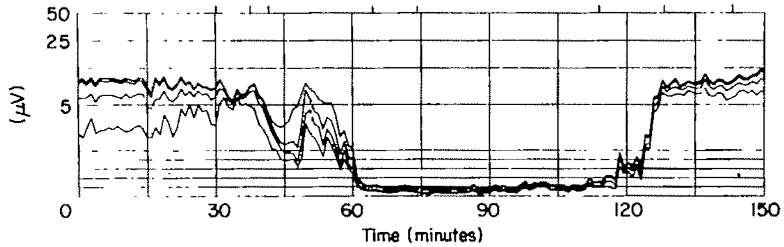


Fig. 3. EEG analysis of a child undergoing open heart surgery during circulatory arrest with profound hypothermia (17°C). Initial phase of bypass—38 to 60 minutes. Final phase of bypass—115 to 143 minutes.

shown in figure 1c. The child was cooled to a core temperature of 17°C, and was operated on under total circulatory arrest (Fig. 3). Immediately prior to the period of circulatory arrest, thiopentone was given and the EEG level fell to less than 1 μV (1 μV was the level of system noise). At the end of bypass, the EEG levels began to return to normal as the body temperature tended towards 37°C (Figs 1, 2 and 3).

In two patients out of the 30 studied, it was noted that spontaneous movements associated with 'lightening' of anaesthesia could be correlated with EEG frequency and amplitude levels changing erratically throughout bypass. The results for one patient are illustrated in Fig. 4.

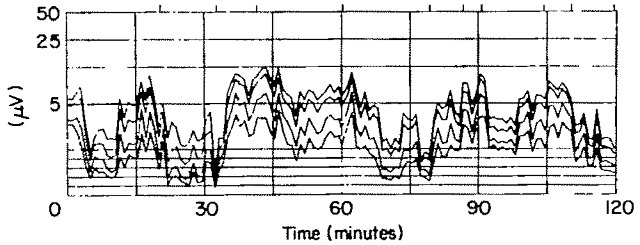


Fig. 4. EEG analysis of an adult undergoing open heart surgery. This patient exhibited spontaneous movements associated with 'lightening' of anaesthesia.

Discussion

Many of the observations made in this report are in agreement with other workers. Kritikou and Branthwaite[2] observed frequent EEG changes in patients immediately following institution of cardiopulmonary bypass. Many of these changes were particularly noticeable in children. Reasons for these changes have been suggested, and include decreased cerebral perfusion, rapid patient cooling, microemboli, hypotension, and effects of bypass prime. Changes with temperature are well recognised. Hicks and Poole[12] divided the effects of body temperatures into a number of bands; between 37 and 35°C there was no discernible change, below 35°C there was progressive slowing of the dominant rhythm, below 29°C there was a large increase in slow activity and a fall in fast activity, and below 18°C all activity ceased. The observations presented here broadly agree with these findings. In the child cooled to 17°C, the EEG fell to less than 1 μV.

The largest changes in this study were seen in children, both at the beginning of bypass and throughout bypass (Fig. 1 and Table 1). Adult patients tended to have slower changes in EEG during bypass, probably as a result of slower temperature changes during the procedure. In addition, the children all received (in relationship to their body weight) much greater volumes of prime (Table 1). The children reached their minimum EEG amplitude faster than the adults. In two of the cases presented here, there were noticeably faster low delta changes and these were both in children (Table 1). It must be stressed that the analysis relating to patient data was retrospective. Nevertheless, the correlates made here are in agreement with other authors.[2,12]

Although equipment for monitoring both EEG frequency and EEG amplitude is now commonly available, there is as yet no large body of evidence suggesting that frequency does vary without amplitude changes, and vice versa. Recently, Maynard and Jenkinson[6] were able to conclude that 'there is incidental evidence that in some circumstances EEG amplitude changes seem independent of EEG frequency distribution'. This study has demonstrated major frequency changes with little or no overall amplitude changes, thus giving weight to the increased use of equipment which analyse in both the amplitude and frequency domains.

References

1. Prior PF. *Monitoring cerebral function. Long term recordings of cerebral electrical activity.* Amsterdam: Elsevier/North Holland Biomedical Press, 1979.
2. Kritikou PE, Branthwaite MA. Significance of changes in cerebral electrical activity at onset of cardiopulmonary bypass. *Thorax* 1977; **32:** 534–8.
3. Sotaniemi KA, Sulg IA, Hokkanen TE. Quantitative EEG as a measure of cerebral dysfunction before and after open-heart surgery. *Electroencephalography and Clinical Neurophysiology* 1980; **50:** 81–95.
4. Maynard DE, Prior PF, Scott DF. Device for continuous monitoring of cerebral activity in resuscitated patients. *British Medical Journal* 1969; **4:** 545–6.
5. Bickford RG, Brimm J, Berger L, Aung M. Application of compressed spectral array in clinical EEG. In: Kellaway P, Petersen I. eds. *Automation of clinical electroencephalography.* New York: Raven Press, 1973; 55–64.
6. Maynard DE, Jenkinson JL. The cerebral function analysing monitor (CFAM). *Anaesthesia* 1984; **39:** 678–90.
7. Klein FF, Davis DA. The use of the time domain analysed EEG in conjunction with cardiovascular parameters for monitoring anaesthetic levels. *IEEE Transactions on Biomedical Engineering* 1981; **28:** 36–40.
8. Hjorth B. Time domain descriptors and their relation to a particular model for generation of EEG activity. In: Dolce G, Kunkel H, eds. *CEAN, computerised EEG analysis.* Stuttgart: Gustav Fischer Verlag, 1975; 3–8.
9. Pronk RAF. *EEG processing in cardiac surgery.* TNO report R-1982-1. Utrecht: Insitute of Medical Physics, 1982.
10. Glaria AP, Murray A. Comparison of EEG monitoring techniques: an evaluation during cardiac surgery. *Electroencephalography and Clinical Neurophysiology*, 1985; 323–30.
11. Glaria AP, Murray A. Development of dynamic display for cerebral function analysis and its use during open heart surgery. *Clinical Physics and Physiological Measurement* 1983; **4:** 455–9.
12. Hicks RG, Poole JL. Electroencephalographic changes with hypothermia and cardiopulmonary bypass in children. *Journal of Thoracic and Cardiovascular Surgery* 1981; **81:** 781–6.

Anaesthesia, 1986, Volume 41, pages 178–180

Anaphylactoid reaction complicating neonatal anaesthesia

E. M. M. POLLOCK, A. D. MACLEOD AND L. R. MCNICOL

Summary

A three-week-old girl presented for surgery for congenital pyloric stenosis. The anaesthetic technique included intravenous induction with thiopentone and neuromuscular blockade with atracurium. The administration of these drugs was followed within 2–3 minutes by oedema of the eyelids and epiglottis, reduced peripheral circulation and central cyanosis.

There was no previous exposure to either drug and no definite family history of allergy. Analysis of subsequent sequential blood samples indicated that the reaction mechanism was non-immune and was presumed to be due to pharmacological release of histamine.

Key words
Allergy.
Neuromuscular relaxants; atracurium.

Case history

A three-week-old girl of normal birthweight was referred for surgery for pyloric stenosis. Following an uneventful pregnancy, her mother had been delivered at term by low cavity forceps under epidural analgesia.

On the 2 days preceding the operation she received nothing orally and only intravenous N/4 sodium chloride/5% dextrose solution with potassium supplements. The stomach was drained via a nasogastric tube. The pre-operative fluid balance was assessed clinically to be satisfactory, and values for venous urea and electrolytes and capillary blood gases were within normal limits. Her weight was 2.6 kg and premedication of 50 μg of atropine was given intramuscularly 2 hours pre-operatively.

At operation there was good intravenous access via a scalp vein through which N/4 sodium chloride/5% dextrose was infused. On aspiration, 1 ml of fluid was obtained from the nasogastric tube. After 3 minutes pre-oxygenation, anaesthesia was induced intravenously with 5.75 mg/kg body weight of thiopentone (15 mg) which was flushed in with 1 ml of infusion fluid. When the eyelash reflex was lost, atracurium, diluted to 1 mg/ml (0.5 mg/kg, 1.3 mg) was administered over approximately 30 seconds. This was flushed in as before and the child's lungs were manually ventilated with 60% nitrous oxide in oxygen.

After 2 minutes, relaxation was judged to be inadequate since there was continuing respiratory effort, coughing and hiccoughing. A further 0.25 mg of atracurium was given and flushed through as before. One minute later, the child was well relaxed and the lungs were easily inflated, so intubation was attempted. On laryngoscopy, the nasopharynx was clear but the vocal cords could not be visualised because the epiglottis was enlarged and swollen and the aryepiglottic folds were oedematous. The infant rapidly developed

---

E.M.M. Pollock, FFARCS, Senior Registrar, A.D. MacLeod, MB, ChB, Registrar, L.R. McNicol, FFARCS, Consultant, Division of Anaesthesia, Royal Hospital for Sick Children, Yorkhill, Glasgow G3 8SJ.

0003–2409/86/020178 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

cyanosis and the heart sounds became feeble on auscultation, although the heart rate as measured by the electrocardiogram remained in excess of 100 beats/minute. One hundred percent oxygen was administered by positive pressure ventilation via a facemask. The chest had undoubtedly become more difficult to inflate and the colour remained dusky.

At this point it was observed that considerable oedema of the eyelids had developed. On the second attempt, a 3.5 mm tracheal tube was passed, and the lungs could be inflated more easily, with good air entry. There was no audible bronchospasm. Fifty millilitres of N/4 sodium chloride/5% dextrose was rapidly infused. Over the next few minutes the cyanosis resolved, the peripheral circulation improved and the heart sounds became louder with a rate of 180 beats/minute. Blood pressure, measured by a neonatal automatic blood pressure recorder (Dinamap, Critikon) was 75 mmHg systolic. Anaesthesia was maintained with 60% nitrous oxide and 0.5% halothane in oxygen. A single intravenous injection of 1 mg dexamethasone was given. One hour after the first appearance of oedema, the epiglottis was re-examined and was seen to be virtually normal.

Atropine 60 μg and neostigmine 120 μg were given intravenously and then, when adequate spontaneous ventilation was established, the child was extubated. She displayed no respiratory distress, had a good colour, cried well and moved vigorously. Direct laryngoscopy confirmed that the vocal cords were easily visualised, moved normally and were only slightly oedematous. She was admitted to the neonatal surgical intensive care unit and observed for the next 24 hours. Treatment comprised maintenance intravenous fluids and humidified oxygen. The subsequent postoperative recovery was uneventful.

Venous samples were taken for immunological analysis at 30 minutes and 3 hours following the reaction. The results were: IgG 5.7 g/litre, IgA 0.2 g/litre, IgM 0.3 g/litre and IgE < 5 i.u./ml. The complement profile was normal.

The child's parents were subsequently interviewed. The mother's sister was possibly allergic to penicillin and some man-made fibres. There was no other family history of note.

Discussion

It is thought that any one of four mechanisms may be responsible for adverse reactions to induction agents and muscle relaxants.[1] First, there is the type I hypersensitivity reaction which is true anaphylaxis. The reaction involves IgE though usually it does not involve complement and previous exposure to the agent is required. Second, there are those immune reactions involving other immunoglobulins, with histamine release via activation of the complement pathway. Third, there may be activation of the alternate complement pathway which may occur on first exposure. Finally there is pharmacological release of histamine.

The infant had had no previous exposure to either thiopentone or atracurium and the immunoglobulin levels were within normal limits for 3 weeks of age,[2] which in association with a normal complement profile, suggested that the mechanism of this reaction was non-immune and was due to pharmacological release of histamine. When such a reaction is as severe as that which occurred in our patient, it is described as 'anaphylactoid'. In general, barbiturate reactions represent immediate antibody-mediated hypersensitivity reactions in patients who have already received several uneventful exposures to the drug.[3] The incidence of the various mechanisms of reaction involving thiopentone has been reviewed, and it is suggested that complement is involved in 59% of cases and antibodies are involved in 77% of cases. However, in 24% of cases the mechanism is pharmacological.[3]

The total dose of atracurium given to this child was 1.55 mg (approximately 0.6 mg/kg. This is within the range of dosage used in paediatric anaesthesia. For instance, in a previous study on the use of atracurium a dose of 0.6 mg/kg ± 10% was used;[4] however, that study did not include neonates. Another report of the use of atracurium in children[5] suggests that there is a 32% incidence of cutaneous reactions, indicating some histamine-releasing effect. However, these cutaneous manifestations are not accompanied by other signs of histamine release such as were were present in our patient and, in 26%, occurred after induction with thiopentone, thus suggesting the possibility of a thiopentone/atracurium interaction when the drugs were given in rapid succession. It is known that histamine release due to atracurium is age-dependent; it is more common in older children and adults than in the young.[6]

Pharmacological release of histamine is more likely to occur when an inappropriately high concentration of drug is given and it is also dependent on the speed of administration.[1] In the case reported here, it may be argued that the dose of atracurium was excessive, since a recent report by Brandom[7] suggests that the ED 95 of this drug in four-week-old infants is 156 μg/kg and our patient received ED 95 × 3 as an intubating dose. However, the same authors found only minimal changes in blood pressure at ED 95 × 5 and no histamine release. Such release of histamine may present in two ways: either predominantly with severe bronchospasm and a degree of cardiovascular collapse, or alternatively, as with our patient, the presentation may be mainly with circulatory collapse. This is due to peripheral vasodilatation and relative hypovolaemia as a consequence of transudation of intravascular fluid through damaged capillaries; laryngeal oedema is a feature in extreme cases.[8]

We have reported this patient to the Committee on Safety of Medicines as a case of adverse reaction to anaesthesia involving thiopentone and atracurium.

Acknowledgments

We are very grateful to Dr J. Watkins of the Royal Hallamshire Hospital, Sheffield, for performing immunological analyses on the blood samples from our patient.

References

1. WATKINS J. Anaphylactoid reactions to I.V. substances. *British Journal of Anaesthesia* 1979; **51:** 51–60.
2. HAYWARD AR, HARBECK R. Tests of specific immunity serum immunoglobin measurements. In: Soothill JF, Hayward AR and Wood CBS. (eds). *Paediatric immunology*. Oxford: Blackwell Scientific Publications, 1983: 462–3.
3. WATKINS J. Hypersensitivity reactions to drugs and other substances. Scurr CF, and Feldman SA (eds). *Scientific foundations of anaesthesia*. 3rd ed. William Heinemann Medical Book, 1982: 520–1.
4. NIGHTINGALE DA, BUSH GH. Abstracts of papers. Atracurium Symposium, The Royal College of Surgeons of England, R. Hughes (ed.). *Atracurium in paediatric anaesthesia.* London 1982: Paper 5.2.
5. LAVERY GC, MIRAKHUR RK. Atracurium besylate in paediatric anaesthesia. *Anaesthesia* 1984; **39:** 1243–6.
6. NIGHTINGALE DA, BUSH GH. Atracurium in paediatric anaesthesia. (Short communication). *British Journal of Anaesthesia* 1983; **55:** 115S.
7. BRANDOM BW, WOELFEL SK, COOK DR, FEHR BL, RUDD DG. Clinical pharmacology of atracurium in infants. *Anesthesia and Analgesia* 1984; **63:** 309–12.
8. FISHER M McD. Blood volume replacement in acute anaphylactic cardiovascular collapse related to anaesthesia. *British Journal of Anaesthesia* 1977; **49:** 1023–6.

Anaesthesia, 1986, Volume 41, pages 181–185

CASE REPORT

All that wheezes is not asthma

A. R. LLOYD-THOMAS AND G. H. BUSH

Summary

A case is presented in which the inhalation of a foreign body caused a respiratory arrest and was subsequently diagnosed and treated as an attack of acute asthma. The presentation, diagnosis, investigation and treatment of this condition is discussed and a review of the literature is presented.

Key words

Complications; asthma, foreign body.

The incidence of foreign body inhalation by children is unknown. It has been reported in 1970 to have caused 2000 deaths per annum in the USA,[1] and, as such, is a significant cause of mortality. Delay in diagnosis is a contributory factor in both the morbidity and mortality.[2] Awareness and team-work by anaesthetists, physicians and surgeons involved in the management of these children will help to reduce the morbidity of this condition.

Case history

A 14-month-old male twin infant was admitted with an 18-hour history of pyrexia and increasing cough. Apart from a very strong family history of atopy, namely asthma and eczema, there was no other significant history. On questioning, both parents were adamant that the child had not had access to any objects sufficiently small to be inhaled. The clinical findings were a pyrexia (38.3°C), tachypnoea (60 breaths/minute), some intercostal recession and a few coarse crepitations audible at the left lung base. A chest X ray on inspiration showed lingual consolidation (Fig. 1).

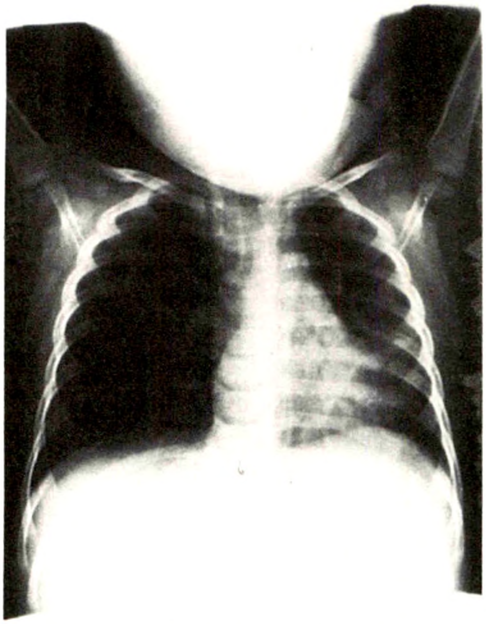


Fig. 1. A-P Chest X ray, taken on the first admission, showing lingual lobe collapse

---

A.R. Lloyd-Thomas*, MB, FFARCS, Registrar, G.H. Bush, DM, FFARCS, Consultant, Alder Hey Children's Hospital, Eaton Road, Liverpool L12 2AP.

*Present address: Department of Anaesthesia, Saint Bartholomew's Hospital, London EC1A 7BE.
Correspondence should be addressed to Dr. G.H. Bush please.

0003–2409/86/020181 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

A leucocytosis with marked neutrophilia was present (WBC 37.0, N 75%, L 14%, M 7%). A diagnosis of pneumonia was made. Humidity, physiotherapy, antibiotics (amoxycillin) and paracetamol were prescribed. Over the next 18 hours, all the clinical signs disappeared, the child became apyrexial and his general condition was much improved. His parents were very anxious to take him home, and this was allowed with an early (4 days) outpatient appointment.

However, 3 days after discharge he presented as an emergency. The night before this admission he had been slightly wheezy, but otherwise well. Twenty minutes before his arrival at the hospital, whilst playing, he had a paroxysm of coughing which ended in apnoea. He became cyanosed, but was given effective mouth to mouth resuscitation by his father, and started to breathe again after 2 minutes.

A history of a foreign body was sought with a further negative reply. The clinical findings were a pyrexia (37.6°C), a tracheal tug, marked inter- and subcostal recession, tachypnoea (50 breaths/minute), bilateral hyperinflation, poor air entry and widespread wheeze. There was no stridor. A chest X ray (Fig. 2) showed bilateral hyperinflation, no areas of collapse or radio-opaque foreign body.

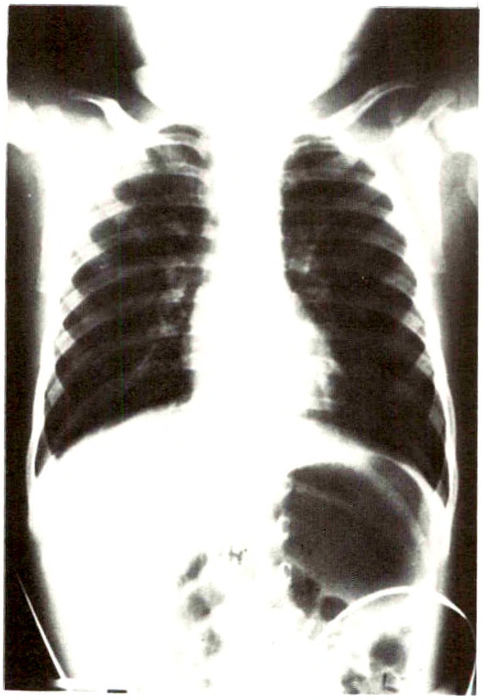


Fig. 2. A-P Chest X ray, taken during the second admission, showing bilateral hyperinflation of the lungs.

Asthma was diagnosed and bronchodilator therapy begun with intravenous hydrocortisone, aminophylline and nebulised salbutamol. The child was kept in humidified oxygen (F_{IO_2} 0.4) and showed significant improvement on this therapy. Twentyfour hours after admission, despite adequate bronchodilator therapy, he deteriorated, becoming restless, distressed, with a tachycardia (200 beats/minute), tachypnoeic (80 breaths/minute), with worsening air entry and consequent diminution of wheeze. His chest X ray remained unchanged and he was referred for bronchoscopy to exclude a foreign body.

After pre-oxygenation and gastric emptying via an *in situ* nasogastric tube, atropine (25 μg/kg) was given intravenously. Anaesthesia was induced with thiopentone (5 mg/kg) and relaxation provided by suxamethonium (1.5 mg/kg). Preliminary oral intubation was performed, anaesthesia was maintained with nitrous oxide (60%) in oxygen (40%) and relaxation with intermittent doses of suxamethonium. Monitoring, with an electrocardiograph and Dinamap blood pressure recorder, was continued. A 3.5 ventilating Storz bronchoscope was passed. The upper airway was normal, but sitting astride the carina was the calyx of an orange surrounded by secretions; this was all removed using a Dormia basket (Fig. 3). The remainder of the tracheobronchial tree was normal.

On recovering from anaesthesia all his respiratory distress and wheeze had gone. Within a few hours he was back to his normal self. Subsequent discussion with the parents revealed that they did not keep oranges in their house, but his grandparents did and he had visited them the day before his first admission.

Discussion

Epidemiology

The majority of children (approximately 80%) who inhale foreign bodies are less than 4 years of age.[1-6] The age group at highest risk is between 12 and 24 months.[3,5,7] At this age many objects are put into the mouth, and being without molar teeth these children possibly do not chew edibles finely enough to swallow them.[8] The male to female ratio is 2:1,[1-3,5,7] a fact attributed to the greater adventurousness of boys.[2]

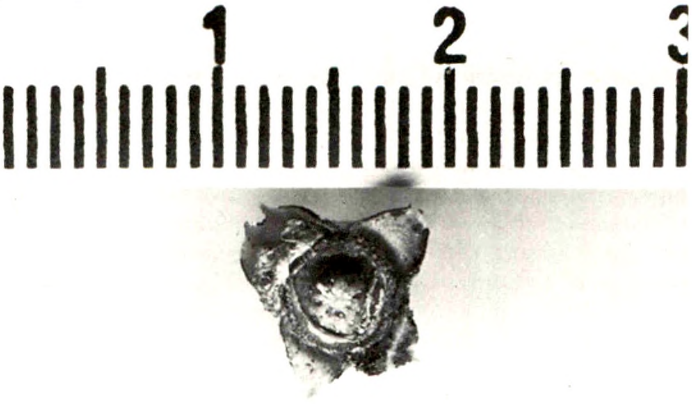


Fig. 3. The calyx of an orange which was removed at bronchoscopy.

Presentation

A clear history of inhalation, usually a variable period of choking, coughing, or gagging, is given in 80–90% of cases.[3,5] However, direct questioning is essential as some guardians may ignore or forget the symptoms of the initial inhalation.[2] If the inhalation is missed, then a latent period may occur, causing a delay in diagnosis.[2] This latency is due to sensory receptors within the respiratory tract adapting to the pressure of a foreign body. Cough will not occur until they are stimulated again either by movement of the foreign body or, more commonly, by the production of secretions which seep up the airways.[2] Even so, 66% of children have the diagnosis made within 1 week, and the majority (64%) of those are made on day one.[9]

Pyman[2] describes six broad categories of clinical presentation as a result of inhalation. Most common (54%) is the sudden onset of wheeze with or without a cough and often with associated evidence of air trapping. These symptoms occur equally frequently in tracheal as well as bronchial foreign bodies. Secondly, there is the presence of cough alone (26%), with or without a pyrexia and other respiratory symptoms. This type of presentation was almost exclusively confined to bronchial foreign bodies. Thirdly, stridor (8.6%) which was only seen in cases where the foreign body was trapped in the subglottis or larynx. Fourthly, haemoptysis (5.6%) which may be the result of a recently inhaled sharp object or the result of a long latent period with the formation of an abscess or bronchiectasis.[10] Threatened asphyxia is the fifth category (5.2%). This can result from the inhalation of a large foreign body which suddenly causes severe obstruction or in those patients with a pneumonia caused by an undiagnosed foreign body that then moves from its site of impaction to cause intense tachypnoea and cyanosis. Finally, as many as 6.5% of his patients were asymptomatic. These patterns of presentation are substantiated by other series.[3,5]

Pathophysiology

Chatterji and Chatterji have described four types of valvular obstruction in bronchial foreign bodies,[11] namely the stop, check, ball and bypass valves. The stop and check valves are the most common; the former cause collapse and the latter obstructive emphysema, of the lung distal to the site of impaction. Foodstuffs comprise 90% of foreign bodies,[3–5,7] with water-melon seeds most common in Kuwait[4] and Turkey;[5] peanuts are most frequent in other series. Vegetable matter tends to swell with bronchial secretions and by doing so may convert a bypass or check valve into a stop valve. Allergenic ('wheezy') or chemical bronchitis may result from absorption of antigenic proteins, organic acids and oils.[5]

Site of lodgement

The right main bronchus is the most common site for foreign bodies to lodge (42–70%), with the left main bronchus the next most frequent

(19–38%).[2,3,5] Lobar lodgement is much less frequent: Blazer *et al.*[3] reported a 9% incidence whilst Pyman[2] reported only a few cases in which small objects such as grass seeds had entered lobar bronchi. Laryngeal (8.7%) and tracheal foreign bodies (5.6%) are much less common, but the latter are more common in children older than 4 years. This is due to the relative smallness of the younger child's larynx and subglottis, in which the larger foreign bodies would be trapped.

Radiological findings

As would be expected, with the large proportion of foodstuffs inhaled, only 6–8% of foreign bodies are radio-opaque.[4,5] In children with bronchial foreign bodies, Blazer *et al.*[3] reported 61% of chest X rays with evidence of obstructive emphysema, 48% with pneumonia or atelectasis and 25% whose X rays were normal. In contrast, 61% of their patients with laryngotracheal foreign bodies had normal chest X rays. Pyman relates his radiological findings to their clinical category of presentation.[2] Of those patients who had bronchial foreign bodies and wheeze as their major symptom, 87% had evidence of obstructive emphysema, whereas of those patients with bronchial foreign bodies and cough as their major symptom, 74% had radiological evidence of lung collapse. Osama *et al.*[4] are the only authors to report a specific subgroup (3% of their patients) with bilateral hyperinflation from obstruction. In their patients, the cause was always a tracheal foreign body.

Good quality inspiratory and expiratory radiographs are essential in revealing all cases of obstructive emphysema.[2,7] Clearly, as 16% of children with bronchial and 61% of children with laryngotracheal foreign bodies have normal chest X rays, plain radiographic examination has its limitations.[3] Fluoroscopy to look for inspiratory widening or an inspiratory shift of the mediastinal shadow increased the success rate of radiological diagnosis of bronchial foreign bodies, from 62 to 92%.[3]

Management

A high index of suspicion is essential in any child less than 4 years of age who presents with the sudden onset of a respiratory illness, even in the absence of a positive history. Our patient was in the highest risk group, being male and 14 months of age. Although to his parents' knowledge he had not played with objects small enough to be inhaled, one must assume that the calyx of the orange fell off while he had that part of the fruit in his mouth. On his first admission, the lack of a positive history, the isolated lingual collapse and the rapid improvement with antibiotics all disguised the underlying foreign body. Only a few foreign bodies reach lobar bronchi, as discussed above, and as such our patient was unusual.

Burrington and Cotton[7] have reported an 80% success rate in clearing the airway of foreign bodies, within 24 hours, by postural drainage, physiotherapy and inhalations of isoprenaline. Other than this specific therapy, the rate of exhalation of bronchial foreign bodies is only 1–2%.[11] However, Cotton *et al.*[12] in a subsequent paper, report two cases of cardiorespiratory arrest in children receiving this therapy. They postulate that 'degassing' of the ipsilateral lung and acute occlusion of the contralateral bronchus by dislodgement of the foreign body caused the circulatory collapse in these children. Acute glottic obstruction or severe reflex bronchospasm are other potential causes. Dislodgement of this kind may have been responsible for the collapse of our patient at home.

A foreign body and not asthma should be suspected when the illness is sudden, there has been no history of previous attacks, no previous coryzal symptoms, no family history and rhonchi are not generalised throughout the chest.[9] However, our patient had been wheezy the night before collapsing, there had been recent evidence of infection, there was a very strong family history, rhonchi were audible throughout the chest and both clinically and radiologically there was evidence of bilateral hyperinflation. These factors supported the diagnosis of asthma.

As discussed above, check valve obstruction of both major bronchi is very unusual, and has only been specifically reported in one previous series.[4] To our knowledge, there have been no specific reports of foreign bodies astride the carina, causing bilateral obstructive emphysema. An alternative explanation would be that the dislodgement had produced severe reflex bronchospasm.[2] However, we feel that this is unlikely, as, if this were the case, it is surprising that all symptoms of respiratory distress were relieved immediately after the removal of the calyx. Instrumentation of the airway might even have been expected to cause further bronchospasm.

However, the failure of bronchodilator therapy to produce a significant improvement should have prompted an earlier bronchoscopy.

In conclusion, it must be remembered that 'all that wheezes is not asthma'.[13] In cases where the inhalation of a foreign body is a possibility, early bronchoscopy is the treatment of choice.[1-5,8,10,12,14] A high index of suspicion is necessary even in the absence of a positive history. With improved paediatric anaesthetic and bronchoscopic techniques the mortality and morbidity of this procedure in specialised paediatric centres is low.[2]

Acknowledgments

We are grateful to Dr J. Martin, under whose care this patient was admitted, for his help and cooperation.

References

1. Friedberg SA, Bluestone GD. Foreign body accidents involving the air and food passages in children. *Otolaryngologic Clinics of North America* 1970; **3:** 395–403.
2. Pyman C. Inhaled foreign bodies in childhood: a review of 230 cases. *Medical Journal of Australia* 1971; **1:** 62–8.
3. Blazer S, Naveh Y, Friedman A. Foreign body in the airway: a review of 200 cases. *American Journal of Diseases of Children* 1980; **134:** 68–71.
4. Abdulmajid OA, Ebeid AM, Motaweh MM, Kleibo IS. Aspirated foreign bodies in the tracheobronchial tree: a report of 250 cases. *Thorax* 1976; **31:** 635–40.
5. Aytac A, Yurdakul Y, Ikizer C, Olga R, Saylam A. Inhalation of foreign bodies in children: a report of 500 cases. *Journal of Thoracic and Cardiovascular Surgery* 1977; **74:** 145–51.
6. Fried MP. Controversies in the management of supraglottitis and croup. *Pediatric Clinics of North America* 1979; **26:** 931–42.
7. Burrington JD, Cotton EK. Removal of foreign bodies from the tracheobronchial tree. *Journal of Pediatric Surgery* 1972; **7:** 119–22.
8. Kim IG, Brummitt WM, Hymphry A, Siomra SW, Wallace WB. Foreign body in the airway: a review of 202 cases. *Laryngoscope* 1973; **83:** 347–54.
9. Williams HE, Phelan PD. Pulmonary complications of inhalation. In: *Respiratory illness in children*. Blackwell, 1975; 237–60.
10. Welch KJ. Bronchiectasis and lung abscesses. In: *Pediatric surgery*. Mustard WT, Ravitch MM, Synder WH. *et al.* (eds) Chicago Illinois Year Book, 1969, pp. 466–88.
11. Chatterji S, Chatterji P. The management of foreign bodies in air passages. *Anaesthesia* 1972; **27:** 390–95.
12. Cotton EK, Abrams G, Vanhoutte J, Burrington J. Removal of aspirated foreign bodies by inhalation and postural drainage. A survey of 24 cases. *Clinical Pediatrics* 1973; **12:** 270–6.
13. Jackson C, Jackson CL. *Foreign body in air and food passages*. New York: Paul B. Hoebner, 1934.
14. Law D, Kosloske AM. Management of tracheobronchial foreign bodies in children: a reevaluation of postural drainage and bronchoscopy. *Pediatrics* 1976; **58:** 362–7.

Anaesthesia, 1986, Volume 41, pages 186–190

CASE REPORT

Amiodarone, phaeochromocytoma and cardiomyopathy

G. SOLARES, F. RAMOS, R. MARTÍN-DURÁN, J. M. SAN-JOSÉ AND M. BUITRAGO

Summary

The anaesthetic management of a patient with a phaeochromocytoma and cardiomyopathy is described. The control of dysrhythmias was the major problem. Ventricular dysrhythmias were treated with lignocaine, and intravenous amiodarone was used to control the supraventricular rhythm disturbances.

Key words

Heart; amiodarone, dysrhythmia.
Surgery; phaeochromocytoma.

Phaeochromocytoma is a rare tumour occurring in 0.4–2 percent of patients with hypertension.[1] The majority of phaeochromocytomata secrete only or predominantly noradrenaline. Phenoxybenzamine and phentolamine are the two agents most commonly used to provide alpha-adrenergic blockade, in order to lower blood pressure and allow intravascular volume expansion. The preoperative management of adrenaline-secreting phaeochromocytomata, especially in those patients who require betablockers for adrenaline-induced symptoms, is under debate.[2] Major concern stems from the development of an unopposed alpha effect, leading to hypertension, pulmonary oedema,[3] shock and death.[4] In addition, negative inotropic effects may precipitate severe heart failure if an associated cardiomyopathy is present.[5]

It has been estimated that approximately 25 percent of patients with a phaeochromocytoma have a concomitant cardiomyopathy.[5] We describe the anaesthetic management of a patient with these entities, and whose major problem was the control of ventricular dysrhythmias in the presence of known compromised cardiac function.

Case history

A 66-year-old, 60 kg male was admitted to hospital by the cardiologist for investigation of his cardiomyopathy. He had been treated with antihypertensive drugs for 8 years. He suffered from attacks of tremor, sweating and palpitations, which had increased over the last 2 years. Blood pressure (BP) was 150/90 mmHg and an apical systolic murmur grade II/VI was present. Apart from this, physical examination revealed no abnormalities. The electrocardiogram demonstrated an enlargement of the left ventricle. Holter monitoring revealed premature atrial contractions (PACs), runs of supraventricular tachycardia

---

G. Solares, MD, Resident of Anaesthesia, F. Ramos, MD, Staff of Anaesthesia, R. Martin-Durán, MD, Staff of Cardiology, J.M. San-José, MD, Staff of Cardiology, M. Buitrago, MD, Anaesthetist in Chief, Departmento Anestesia y Reanimación and Servicio Cardiologia, Hospital Nacional Valdecilla, 39008 Santander, Spain.

Correspondence should be addressed to: Dr R. Martín-Durán, MD, Servicio Cardiologia, Hospital Nacional Valdecilla, 39008 Santander, Spain.

0003–2409/86/020186 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

(SVT), frequent premature ventricular contractions (PVCs) with the so-called R-on-T phenomenon and runs of ventricular tachycardia (VT). A two-dimensional echocardiogram demonstrated marked dilatation of the left ventricle, with impairment of contractility and global hypokinesia. The left atrium was dilated. The mitral, aortic and tricuspid valves appeared structurally normal. Diastolic left ventricular internal dimension (LVIDd) was 69 mm, fractional shortening of the left ventricle (FrSh) was 23 mm and the ejection fraction (EF) was 38 percent. Urinary 24-hour-measurements of vanilylmandelic acid was 19.2–22 mg (normal 0–12 mg), and total free catecholamines was 378 μg (normal 100 μg). Phaeochromocytoma was then suspected. A round mass in the left suprarenal gland was identified by abdominal computerised axial tomography. Phaeochromocytoma together with dilated cardiomyopathy with malignant ventricular dysrhythmias was the final diagnosis.

Phenoxybenzamine 40 mg/day orally was started 14 days before surgery. Prior to anaesthesia, an intravenous continuous infusion of amiodarone 600 mg in 5 percent dextrose solution was maintained for 12 hours. The patient was premedicated with morphine 5 mg, diazepam 5 mg and scopolamine 0.5 mg intramuscularly one hour before operation. A balloon tipped, flow directed, pulmonary artery catheter (7 French gauge) was inserted to determine cardiac output (CO) by thermodilution. Lignocaine 60 mg was necessary to treat a run of VT. During the insertion of a left radial artery cannula under local anaesthesia, arterial BP rose from 150/90 to 180/110 mmHg. An infusion of sodium nitroprusside (SNP) 0.5 μg/kg/minute was started and maintained until tumour removal, and arterial BP decreased to 120/80 mmHg. Induction of anaesthesia was performed with diazepam 25 mg, fentanyl 0.20 mg and pancuronium 6 mg. Another 60 mg of lignocaine was administered. The patient's lungs were ventilated with nitrous oxide: oxygen (50:50) via a facemask for 3 minutes, then his trachea was intubated. Anaesthesia was maintained with nitrous oxide: oxygen (70:30) and supplementary doses of fentanyl and pancuronium. Intravenous infusions of lignocaine and amiodarone 300 mg/in 5 percent dextrose solution were maintained throughout the surgical procedure. During tumour manipulation, several increases in BP occurred and the patient developed a SVT of 140 beats/minute. This was controlled with intravenous amiodarone 300 mg given slowly over a period of 2 minutes. Arterial BP increases were managed using bolus doses of phentolamine (5 mg) on three occasions. After tumour removal arterial BP decreased to 100/50 mmHg but, 10 minutes later, it rose to 170/105 mmHg, and pulmonary capillary wedge pressure (PCWP) was 28 mmHg. No additional tumours were found. Frusemide 10 mg was given, and the SNP infusion was restarted and maintained during the next 24 hours. Replacement of blood loss and intra-operative fluid therapy consisted of 3800 ml in all. Throughout the operation, the dysrhythmias consisted of SVT, frequent PACs and occasionally PVCs. A 4 × 6 × 3 cm mass was removed; histologically it was confirmed as a phaeochromocytoma mainly secreting adrenaline.

Two months later, arterial BP was 140/80 mmHg and total urinary free catecholamines were normal. Holter monitoring demonstrated occasional PVCs. A two-dimensional echocardiogram revealed an improvement in contractility, and a mild decrease of left ventricular dilatation. The patient now enjoys good health.

Discussion

The anaesthetic management of patients with a phaeochromocytoma plus dilated cardiomyopathy should be based on[6,7] the administration of drugs that do not stimulate the sympathetic system, maintenance of normovolaemia, prevention of afterload increases and the avoidance of myocardial depression and, finally, the use of cardiovascular monitoring to ensure an accurate assessment of haemodynamic status.

We selected diazepam and nitrous oxide–fentanyl because of their minimum cardiovascular effects.[7] Enflurane[1] and to a lesser extent, isoflurane produce direct myocardial depression, so their use in the presence of a cardiomyopathy may be unwise.[7] Pancuronium has been proposed as the relaxant of choice,[8,9] although severe hypertension has been associated with its use in a patient with phaeochromocytoma.[10] The administration of droperidol has been reported to produce hypertension and tachycardia in this condition.[11,12] Droperidol seems to stimulate the release of catecholamines from the tumour.[11]

Plasma catecholamine levels are increased during tracheal intubation and tumour manipulation, producing arterial BP increases in spite of pre-operative alpha-blockade.[1] Fentanyl 200 μg and lignocaine 1 mg/kg, reduce the arterial BP response and the likelihood of cardiac dysrhythmias occurring in response to tracheal intubation.[6,13] Phentolamine in small doses is the drug of choice to block the alpha-adrenergic receptors if arterial BP increases occur; tachyphylaxis, however, is its major disadvantage. Continuous administration should not be employed as it may produce unmanageable hypotension after tumour resection.[13] Sodium nitroprusside is a potent vasodilating drug which reduces systemic vascular resistance (SVR) and arterial BP, producing a moderate increase in CO.[14]

Disturbances of the cardiac rhythm were the major difficulty during the anaesthetic management of our patient. The maintenance of a normal arterial BP is basic to minimising the incidence of dysrhythmias,[6,14,15] but if these occur, lignocaine is the drug of choice for ventricular rhythm disturbances. The pre-operative use of propranolol has been recommended when dysrhythmia or angina exist,[13,16] and peroperative use is necessary if significant supraventricular tachycardia appears. Nevertheless, its use in our case is open to question for several reasons. It is known that it may trigger pulmonary oedema,[3] shock and death[4] in patients with phaeochromocytoma without prior alpha-blockade. Furthermore, complete atrioventricular block with post-operative death,[16] and hypoglycaemia after tumour resection,[14] have been reported. Theoretically, the beta-adrenergic effects of the elevated catecholamine levels are responsible for the cardiomyopathy and blockade of these effects could be beneficial to cardiac function. Nevertheless, it is the opinion of some authors that the use of propranolol in this condition can accentuate left ventricular dysfunction.[6,7] Furthermore, it has been suggested that the administration of beta-adrenergic blockers in dilated cardiomyopathy should be considered speculative, experimental and potentially dangerous.[17,18] This point of view has been confirmed by the recently reported fact that propranolol precipitated left heart failure with pulmonary oedema in a patient with a phaeochromocytoma plus cardiomyopathy under alpha-adrenergic treatment.[5]

Amiodarone is a benzofuran derivative, originally introduced as an anti-anginal drug.[19] It soon became established as an antidysrhythmic agent for treating supraventricular[20] and ventricular[21] tachydysrhythmias, but without having a significant negative inotropic effect in the normal or failing heart.[22] Amiodarone produces a noncompetitive adrenergic blockade,[23] reducing the effect of sympathetic stimulation and catecholamines in both alpha- and beta-adrenergic receptors.[23,24] It produces a decrease of SVR, reducing the afterload.[25] Amiodarone inhibits isoprenaline-induced tachycardia by about 50 percent, in the right atria of rabbits.[26] Its electrophysiological action is effected by a prolongation of repolarisation and refractoriness of the sinus node, atrium, atrioventricular node, Purkinje system and ventricle.[27] Some differences have been noted between the electrophysiological effects of amiodarone during intravenous infusion and those found during oral administration.

It has been shown that a dose dependent bradycardia develops when amiodarone is given intravenously to anaesthetised dogs;[28] this is accompanied by a prolongation of the P-R interval, without lengthening of the Q-T interval. The drug has no clinical or haemodynamic side effects in man when injected at 5 mg/kg body weight.[21] In patients with depressed left ventricular function and an EF > 30 percent, amiodarone given intravenously resulted in a decrease in heart rate, but cardiac index and stroke volume index remained unchanged.[29] The pharmacokinetics of amiodarone remain incompletely described but it has a large volume of distribution, a long half life and a low clearance rate.[30] The onset of antidysrhythmic effects after intravenous administration is observed almost immediately, and lasts between 20 minutes and 4 hours.[31] Intravenous amiodarone was effective in controlling over 90 percent of atrial tachydysrhythmias.[32,33] Intravenous amiodarone provided a reduction in the overall rate of ventricular tachydysrhythmias in about 60 percent of patients.[34] Its antidysrhythmic property has been confirmed for both supraventricular and ventricular dysrhythmia during cardiac surgery under neurolept-analgesia; however, a potentiation of sympatholytic alpha effects has been observed.[35] Interactions of amiodarone and anaesthetics, resulting in hypotension and atropine-resistant bradycardia, have been reported in a patient receiving the drug orally.[36]

It has been demonstrated that right-side pressure changes do not reflect left-side pressure changes in patients with phaeochromocytoma.[37] Furthermore, the combination of cardiomyopathy and the potential for large fluid requirements if hypotension occurred after tumour resection, suggested the necessity of monitoring pulmonary capillary wedge pressure and cardiac output. This type of invasive monitoring is not without hazard however; indeed, an intravenous bolus of lignocaine was necessary to control a run of VT during the insertion of the pulmonary artery catheter. We observed an improvement of CO after tumour removal which has been noted previously.[38] Nevertheless, 10 minutes after tumour resection, BP, PcWP and SVR rose. Further catecholamine-secreting tumours have been reported to cause such an increase,[9] but the abdominal cavity was re-examined and none was found. The persistent arterial BP elevation might be explained by the slow release of increased catecholamine stores, or by intra-operative overtransfusion.[39]

In summary, the anaesthetic technique described resulted in the safe management of a patient with a phaeochromocytoma and cardiomyopathy. Ventricular dysrhythmias were treated with lignocaine. We consider that amiodarone is a valid alternative to beta-adrenergic antagonists to control supraventricular tachydysrhythmias in patients with a phaeochromocytoma and an associated cardiomyopathy.

Acknowledgments

The authors thank Dr J.M. Revuelta, and Mr Brian Hunt for their valuable suggestions in preparing the manuscript.

References

1. Vater M, Achola K, Smith G. Catecholamine responses during anaesthesia for phaeochromocytoma. *British Journal of Anaesthesia* 1983; **55:** 357–60.
2. Modlinger R, Ertel NH, Hauptman JB. Adrenergic blockade in pheochromocytoma. *Archives of Internal Medicine* 1983; **143:** 2245–6.
3. Wark JD, Larkins RG. Pulmonary oedema after propranolol therapy in two cases of phaeochromocytoma. *British Medical Journal* 1978; **1:** 1395–6.
4. Sloand EM, Thompson TB. Propranolol-induced pulmonary edema and shock in a patient with pheochromocytoma. *Archives of Internal Medicine* 1984; **144:** 173–4.
5. Gilsanz FJ, Luengo C, Conejero P, Peral P, Avello F. Cardiomyopathy and phaeochromocytoma. *Anaesthesia* 1983; **38:** 880–91.
6. Tasch M. Endocrine diseases. In: Stoelting RK, Dierdot SF eds. *Anesthesia and co-existing disease.* New York: Churchill Livingstone, 1982; 437–83.
7. Hilgenberg JC. Cardiomyopathies. In: Stoelting RK, Dierdot SF eds. *Anesthesia and co-existing disease.* New York: Churchill Livingstone, 1982; 129–33.
8. Janeczko GF, Ivankorvich AD, Glisson SN, Heyman HJ, El-Etr AA, Albrecht RF. Enflurane anesthesia for surgical removal of pheochromocytoma. *Anesthesia and Analgesia* 1977; **56:** 62–7.
9. Csánky-Treels JC, Lawick Van Pabst WP, Brands JWJ, Stamenkovic L. Effects of sodium nitroprusside during the excision of phaeochromocytoma. *Anaesthesia* 1976; **31:** 60–2.
10. Jones RM, Hill AB. Severe hypertension associated with pancuronium in a patient with a phaeochromocytoma. *Canadian Anaesthetists' Society Journal* 1981; **28:** 394–6.
11. Sumikawa K, Amakata Y. The pressor effect of droperidol on a patient with pheochromocytoma. *Anesthesiology* 1977; **46:** 359–61.
12. Bittar DA. Innovar-induced hypertensive crises in patients with pheochromocytoma. *Anesthesiology* 1979; **50:** 366–9.
13. El-Naggar M, Suerte E, Rosenthal E. Sodium nitroprusside and lidocaine in the anaesthetic management of phaeochromocytoma. *Canadian Anaesthetists' Society Journal* 1977; **24:** 353–9.
14. Stamenkovic L, Spierdijk J. Anaesthesia in patients with phaeochromocytoma. *Anaesthesia* 1976; **31:** 941–5.
15. Conner JT, Miller JD, Katz RL. Isoflurane anesthesia for pheochromocytoma: a case report. *Anesthesia and analgesia* 1975; **54:** 419–21.
16. Bingham W, Elliott J, Lyons SM. Management of anaesthesia for phaeochromocytoma. *Anaesthesia* 1972; **27:** 49–60.
17. Braunwald W. *Heart disease.* Philadelphia: WB Saunders Company, 1984; 1406.
18. Ikram H, Fitzpatrick MA. Beta blockade for dilated cardiomyopathy: the evidence against therapeutic benefit. *European Heart Journal* 1983; **4** (Suppl A): 179–80.
19. Vastesaeger M, Gillot P, Rasson G. Etude clinique d'une nouvelle médication antiangoreuse. *Acta Cardiológica* (Belgium) 1967; **22:** 483–500.
20. Rosenbaum MB, Chiale PA, Ryba D, Elizari MV. Control of tachyarrhythmias associated with Wolf-Parkinson-White syndrome by amiodarone hydrochloride. *American Journal of Cardiology* 1974; **34:** 215–23.
21. Rosenbaum MB, Chiale PA, Halpern MS, Nau GJ, Przbylski J, Levi RJ, Lazzari JO, Elizari MV. Clinical efficacy of amiodarone as an antiarrhythmic agent. *American Journal of Cardiology* 1976; **38:** 934–44.

22. Barzin J, Fréson A. Essais cliniques de l'amiodarone dans les affections coronariennes. *Bruxelles Medicale* 1969; **49:** 105–22.
23. Charlier R. Cardiac actions in the dog of a new antagonist of adrenergic excitation which does not produce competitive blockage of adrenoceptors. *British Journal of Pharmacology* 1970; **39:** 668–74.
24. Charlier R, Deltour G, Baudine A, Chaillet F. Pharmacology of amiodarone, an anti-anginal drug with a new biological profile. *Arzneimittelforschung* 1968; **18:** 1408–17.
25. Côté T, Bourassa MG, Delaye J, Janin A, Froment R, David P. Effects of amiodarone on cardiac and coronary hemodynamics and on myocardial metabolism in patients with coronary artery disease. *Circulation* 1979; **59:** 1165–72.
26. Polster P, Broeckhuysen J. The adrengeric antagonism of amiodarone. *Biochemical Pharmacology* 1976; **25:** 131–4.
27. Rosen MR, Wit AL. Electropharmacology of antiarrhythmic drugs. *American Heart Journal* 1983; **106:** 829–39.
28. Singh BN, Jewitt DE, Downey JM. Effects of amiodarone and L8040, novel antianginal and antiarrhythmic drugs, on cardiac and coronary haemodynamics and on cardiac intracellular potentials. *Clinical and Experimental Pharmacology and Physiology* 1976; **3:** 427–42.
29. Schwartz A, Shen E, Morady F, Gillespie K, Scheinman M, Chatterjee K. Hemodynamic effects of intravenous amiodarone in patients with depressed left ventricular function and recurrent ventricular tachycardia. *American Heart Journal* 1983; **106:** 848–55.
30. Holt DW, Tucker GT, Jackson PR, Storey GCA. Amiodarone pharmacokinetics. *American Heart Journal* 1983; **106:** 840–6.
31. Marcus FI, Fontaine GH, Frank R, Grosgogeat Y. Clinical pharmacology and therapeutic applications of the antiarrhythmic agent, amiodarone. *American Heart Journal* 1981; **101:** 480–39.
32. Benaim R, Denizeau JP, Melon J, Domengie B, Kolsky H, Chapelle M, Chiche B. Les effets antiarrythmiques de l'amiodarone injectable. *Archives des Maladies du Coeur* 1976; **69:** 513–22.
33. Benaim R, Luzan C. Les effets antiarrythmiques de l'amiodarone injectable (à propos de 153 cas). *Reviste Médicale Internationale* 1978; **19:** 1959.
34. Singh BN, Collet JT, Chew CYC. New perspectives in the pharmacologic therapy of cardiac arrhythmias. *Progress in Cardiovascular Diseases* 1980; **22:** 243–301.
35. O'Byrne P, Ledouarin B, Loisance B, Rosanval O. Chlorhydrate d'amiodarone et anesthésie en chirurgie cardioque. Utilisation de la forme injectable dans la correction des troubles du rythme peropératoires. *Annales d'Anesthésiologie Française* 1976; **17:** 567–75.
36. Gallagher JD, Lieberman RW, Meranze J, Spielman SR, Ellison N. Amiodarone-induced complications during coronary artery surgery. *Anesthesiology* 1981; **55:** 186–8.
37. Mihm FG. Pulmonary artery pressure monitoring in patients with pheochromocytoma. *Anesthesia and Analgesia* 1983; **62:** 1129–33.
38. Kreul JF, Dauchot PJ, Anton AH. Hemodynamic and catecholamine studies during pheochromocytoma resection under enflurane anesthesia. *Anesthesiology* 1976; **44:** 265–8.
39. Holland, OB, Isselbacher KJ. Pheochromocytoma: surgery. In: Adams RD, Braunwald E, Petersdorf RG, Wilson JD, eds. *Harrison's principles of internal medicine*. 9th edn. New York: McGraw-Hill, 1980; p. 1741.

Anaesthesia, 1986, Volume 41, pages 191–194

CASE REPORT

Anaesthesia for surgical occlusion of the basilar artery

A technique involving intra-operative awakening to allow neurological assessment

C. S. CHILD, M. P. D. HEINING, I. CALDER AND H. A. CROCKARD

Summary

A case is described of a giant fusiform aneurysm of the basilar artery which was treated successfully by proximal surgical occlusion of the artery. The anaesthetic management involved the intra-operative awakening of the patient in order to assess neurological function immediately after application of the clip. The difficulties involved in this type of surgery are discussed.

Key words
Anaesthesia; neurosurgical.

Intra-operative awakening of a patient to allow assessment of neurological function is a useful technique which is used during short procedures, such as percutaneous cordotomy and ablation of the trigeminal ganglion by thermocoagulation,[1] and occasionally during more major operations, such as the insertion of Harrington rods.[2–4] However, the technique has not been described for patients undergoing the clipping of an aneurysm of a major cerebral vessel. We describe here the case of a patient with a giant fusiform aneurysm of the basilar artery, in whom intra-operative awakening was performed to allow neurological assessment after clipping of the aneurysm. The problems involved in allowing a patient to awaken from anaesthesia whilst the skull and dura are open are discussed.

Case history

The patient was an intelligent and alert 16-year-old Egyptian girl who spoke little English. She had a 4-year history of headaches of increasing frequency, recent onset of nausea and vomiting, and pain in the left eye and right ear. Computerised tomography revealed a space-occupying lesion of the anterior part of the posterior fossa (Fig. 1) and angiography showed a fusiform aneurysm of the basilar artery (Fig. 2). It was decided to occlude the basilar artery surgically and to wake the patient intra-operatively, immediately after clipping the artery, in order to assess neurological function.

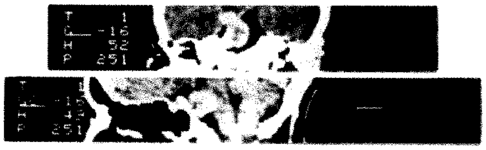


Fig. 1. Computerised tomography showing the presence of aneurysm.

C.S. Child, FFARCS, Senior Registrar, M.P.D. Heining, FFARCS, Senior Registrar, I. Calder, FFARCS, Consultant, H.A. Crockard, FRCS, Consultant, The National Hospital for Nervous Diseases, Maida Vale, London W9 1TL.
Correspondence should be addressed to: Dr C.S. Child, Department of Anaesthesia, University College Hospital, Gower Street, London WC1E 6AU.

0003–2409/86/020191 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

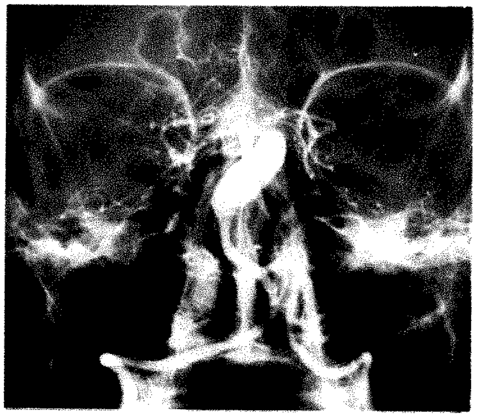


Fig. 2. Pre-operative angiogram revealing a giant fusiform basilar artery aneurysm.

Morphine 10 mg and dexamethasone 8 mg were administered intramuscularly one hour preoperatively. Anaesthesia was induced with thiopentone 400 mg and intubation of the trachea with an 8-mm Portex tube was performed after suxamethonium 100 mg and spraying of the vocal cords with lignocaine. The patient was placed in the 'park bench' position on the operating table. Anaesthesia was maintained with nitrous oxide and oxygen using tubocurarine 35 mg for muscle relaxation. Droperidol 5 mg and papaveretum 10 mg were given intravenously before the start of surgery and enflurane 0.5 percent was administered until the dura was opened. Blood pressure was monitored directly from the radial artery and the ECG and end-tidal carbon dioxide level were continuously displayed. Auditory-evoked cortical responses were monitored throughout the procedure. The systolic blood pressure was reduced to 80 mmHg for the period of application of the clip, using an infusion of sodium nitroprusside. Clipping of the artery took place approximately one and a half hours after the induction of anaesthesia.

Immediately following the application of the clip, the nitroprusside was discontinued, the patient's lungs were ventilated with 100% oxygen and neostigmine 2.5 mg and atropine 1.2 mg were given intravenously. Spontaneous ventilation had not returned after five minutes, despite an end-tidal carbon dioxide level of more than 5.33 kPa. Intravenous naloxone was therefore given in increments of 0.05 mg to a total dose of 0.2 mg, when the desired response was achieved. Within 10 minutes, the patient had restarted spontaneous ventilation and within 15 minutes she had moved all limbs and had squeezed the hand of the anaesthetist to command. She would not, however, open her eyes to command so it was impossible to assess her sight. The patient's cardiovascular system remained stable and the auditory-evoked cortical responses remained unchanged after application of the clip. Her responses were judged to be satisfactory, so, 160 minutes after the original induction of anaesthesia, she was re-anaesthetised with thiopentone 200 mg and diazepam 5 mg and paralysed with tubocurarine 25 mg. Positive pressure ventilation was re-established and the dura and skull closed. Ventilation was continued until the patient was fully awake and seen to be intact neurologically.

Angiography, three weeks later, confirmed that blood flow though the diseased vessel had ceased (Fig. 3).

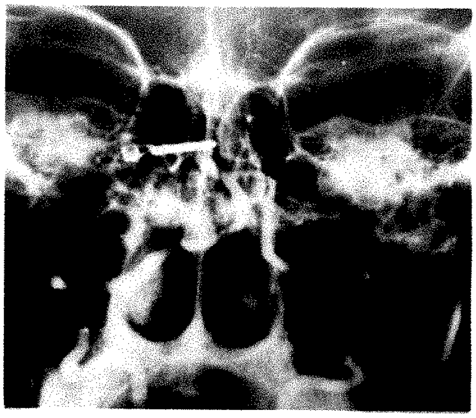


Fig. 3. Postoperative angiogram showing the presence of the clip and confirming the cessation of blood flow through the basilar artery.

Discussion

The basilar artery is formed by the anastomosis of the vertebral arteries and is a major contributor to the circle of Willis (Fig. 4). Branches which come directly from it include the anterior inferior cerebellar, superior cerebellar, pontine, labyrinthine and posterior cerebral arteries. Occlusion of the basilar artery may, therefore, be responsible for widespread ischaemia, resulting in respiratory and cardiovascular dysfunction, cortical blindness, ataxia and inner ear dysfunction.

Until recently, basilar artery occlusion had

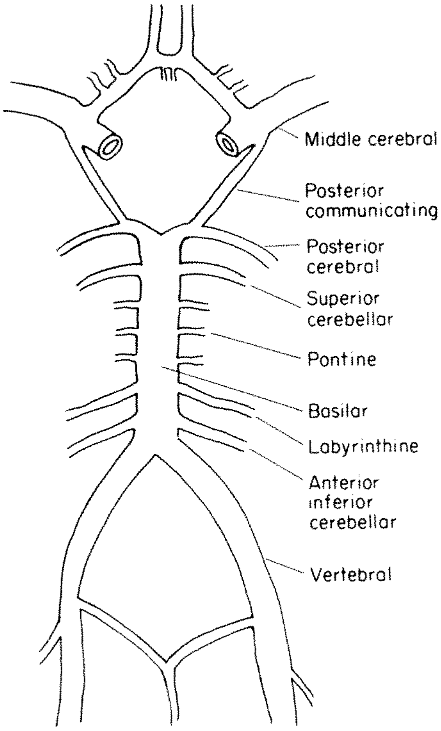


Fig. 4. The circle of Willis.

been thought to be incompatible with life but there have now been reports of spontaneous thrombotic occlusion and surgical occlusion which have been followed by a comprehensive rehabilitation.[5,6] Surgical occlusion of the basilar artery may be performed in cases of giant or fusiform aneurysm in which the neck of the aneurysm cannot be surgically isolated. The occlusion initiates thrombosis of the parent artery and the brain stem is then dependent on collateral flow from the posterior communicating arteries. However, the adequacy of collateral supply is difficult to ascertain pre-operatively and cannot be reliably predicted by angiographic techniques.[6] Intra-operative monitoring may aid the detection of ischaemia, but it is impossible to be certain that the patient will regain consciousness following a surgical occlusion. Changes in cardiovascular function, such as hypotension or bradycardia, may occur when the brain stem is rendered ischaemic but these changes are non-specific. The patient may be allowed to breathe spontaneously to enable respiratory rate, rhythm and depth to be monitored. However, the absence of respiratory changes does not guarantee the absence of neurological damage. Multichannel electroencephalography (EEG) may be useful, especially using the more compact forms of the cerebral function monitor and the cerebral function analysing monitor. However, the EEG is difficult to interpret and may not detect lesions which do not reach the convexity of the brain.[7] Brain stem auditory-evoked potentials are relatively easy to measure, assess subcortical functions and are not affected by anaesthesia. Changes in evoked potentials have been reported to occur in acute ischaemia.[8]

One solution to the problems of basilar artery surgery was suggested by Drake; a snare is placed around the basilar artery and then tightened around the vessel on the day after operation, thus allowing neurological assessment to be made on the awake patient.[6] The problem here is that the snare may be dislodged from the intended site during the postoperative period and that the patient obviously experiences discomfort during the procedure. The patient must then be re-anaesthetised for the artery to be permanently clipped, during a separate operation.

An alternative approach is to perform extracranial–intracranial arterial bypass using the superficial temporal artery to provide collateral flow to the rostral brain stem before occluding the basilar artery.[9] This procedure requires a greater degree of surgical manipulation of the brain than when clipping or snaring and is technically very difficult. There is also no guarantee that the blood flow in the pontine branches of the basilar artery will be preserved once the vessel is occluded. In view of these problems, we elected to wake the patient intra-operatively and to perform an assessment of neurological function immediately after the vessel had been clipped.

The choice of anaesthetic technique for this procedure is a difficult one, as the patient is required to awake quickly but quietly, to remain intubated without coughing and to respond to commands. If violent movements or coughing do occur it is possible that cerebral herniation or disruption of the brain stem may result. It was essential to re-establish spontaneous ventilation during this case in order to assess brain stem function adequately and we considered that the use of neuroleptanaesthesia was likely to reduce the possibility of any violent movements occurring. Techniques which allow intra-operative awakening of the spontaneously breathing, intubated patient have been described for intracranial ablation therapy for chronic pain and Parkinson's disease over twenty years ago[10,11] These involved the use of nitrous oxide, oxygen and halothane with either hydroxydione or pethidine. Awakening is likely to be slow using these techniques, and spontaneous ventilation is considered by many to be inappropriate during hypotensive posterior fossa surgery. Neurolept-anaesthesia using droperidol and fentanyl have been described for the surgical treatment of Parkinsonism,[12] but these did not involve tracheal intubation.

The administration of naloxone and neostigmine to patients being awoken intra-operatively has been described, but is not without its dangers; in one study,[4] this resulted in a patient extubating himself and another required to be restrained on the operating table. It should be used slowly and with caution.

It may be difficult to judge whether the patient is merely slow to awaken from the anaesthesia or whether the collateral blood flow is inadequate. Monitoring of auditory-evoked cortical responses may help in this respect. No changes in evoked potential were seen during this case. We would, however, recommended that if the patient is slow to breathe and is not obeying commands following occlusion of the artery despite a normal or raised end-tidal carbon dioxide level, an adequate perfusion pressure, normal temperature, adequate neuromuscular conduction and antagonism of respiratory depressants by naloxone, then the clip should be removed and Drake's method of delayed occlusion used.

In conclusion, we have demonstrated in this case that the intra-operative awakening of a patient undergoing a craniotomy for vertebro-basilar occlusion therapy of a fusiform basilar artery aneurysm may allow assessment of neurological function following occlusion of the artery.

Acknowledgments

We are grateful to Dr T.R. Abbott and Dr C.G. Drake for their advice and to Miss A. Woolf for her secretarial assistance.

References

1. Lowe SS, Meurer M, Ingram GS, Thomas DT. Anaesthesia for trigeminal nerve thermocoagulation. *Anaesthesia* 1983; **38:** 152–4.
2. Vauzelle C, Stagnara P, Jouviroux P. Functional monitoring of spinal cord activity during spinal surgery. *Clinical Orthopaedics and Related Research* 1973; **1: 93:** 173–8.
3. Abbott TR, Bentley G. Intra-operative awakening during scoliosis surgery. *Anaesthesia* 1980; **35:** 298–302.
4. Hall JE, Levine CR, Sudkir KG. Intra-operative awakening to monitor spinal cord function during Harrington instrumentation and spinal fusion. *Journal of Bone and Joint Surgery*. 1978; **60-A:** 533–6.
5. Weber P, Heuck CC, Zimmerman R. Basilams Thrombase. Ein Beispiel für eine umfassende Rehabilitation bei einer jungen Patientin von 26 jahren. *Rehabilitation* (Stuttgart). 1983; **2:** 76–80.
6. Drake CG. Ligation of the vertebral (unilateral or bilateral) or basilar artery in the treatment of large intracranial aneurysms. *Neurosurgery* 1975; **43:** 255–74.
7. Prior PF. EEG monitoring and evoked potentials in brain ischaemia. *British Journal of Anaesthesia* 1985; **57:** 63–81.
8. Rossi L, Ubiali E, Rottoli MR, Merli R. I Potentiali uditiui evocalti nei T-I-A del circolo posteriore *Rivista Di Veurologia* (Roma) 1983; **2:** 106–15.
9. Hopkins LN, Bundy JL, Castellani D. Extracranial–intracranial bypass and basilar artery ligation in the treatment of giant basilar aneurysm. *Neurosurgery* 1983; **2:** 189–94.
10. Hurter DG. Anaesthesia for thermocoagulation of the globus pallidus. *British Journal of Anaesthesia* 1960; **32:** 160–3.
11. Vourch G, Hardy J, Denavit M. Problems raised by anaesthesia for thalamic and cortical exploration in neurosurgery. *British Journal of Anaesthesia* 1963; **35:** 208–18.
12. Brown AS. Neuroleptanaesthesia for the surgical treatment of Parkinsonism. *Anaesthesia* 1964; **19:** 70–74.

Anaesthesia, 1986, Volume 41, pages 195–197

APPARATUS

A new device for the inflation of the antigravity suit

P. M. BRODRICK

Summary

The 'Schuco' orthopaedic tourniquet inflator can be simply converted into a suitable device for inflating an antigravity suit (G-suit). The antigravity suit may be used on neurosurgical patients undergoing procedures in the sitting position to help prevent hypotension and air embolism. The availability of this device may encourage the more widespread use of an antigravity suit in neuro-anaesthetic practice.

Key words

Complications; hypotension, air embolism.
Equipment; antigravity suit inflator, antigravity suit.

Patients having neurosurgical operations performed in the sitting position are at risk from hypotension, due to the pooling of blood in the extremities.[1] These patients may be at risk from air embolism because of the presence of localised subatmospheric venous pressure at the operation site.[1–4] Nevertheless, this position is still popular in some neurosurgical centres, and so precautions should be taken to avoid these hazards.[5]

One preventive method is to use an antigravity suit.[6,7] When inflated this acts as an artificial peripheral resistance in the lower extremities and the splanchnic regions, which forces blood into the intravascular space above the diaphragm. This produces an increase in venous return and a rise in central venous pressure. There is an increase in mean arterial pressure with a slight fall in cardiac output, due to an associated bradycardia.[8–11] These changes help to reduce the incidence of hypotension and air embolism.[4,6,12]

The use of an antigravity suit (of the aviation type) has been routine in this type of case at the National Hospital for many years. The suit has been inflated by means of a cylinder of compressed air or oxygen attached to a pressure reducing valve, which reduces the pressure to 7 kPa via a two-stage regulator; the second stage is a large rubber diaphragm. Unfortunately, these diaphragms perish easily and supplies have been restricted because lack of demand has caused production to be discontinued. Therefore, an alternative method of inflation of the garment was sought, and this report describes a modification to an orthopaedic tourniquet inflator which can then be used to inflate an antigravity suit.

Methods

The 'Schuco' orthopaedic tourniquet inflator (Model AT500) is normally used for the maintenance of bloodless fields in orthopaedic surgery on the limbs. For that purpose, it is necessary to generate pressures in excess of the systolic blood pressure, and the usual pressure range in adults is approximately 3 and 10 kPa above systolic pressure for the arm and leg respectively. The

---

P.M. Brodrick, MB, BS, FFARCS, Research Fellow, The National Hospital for Nervous Diseases, Queen Square, London WC1.

0003–2409/86/020195 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

inflation source used on this particular model can be either a pipeline supply or a cylinder of compressed gas and a two-stage regulator.

The inflator is housed in a small box approximately 0.325 m × 0.2 m × 0.125 m, which has an attachment on the back so that it can be fixed to an infusion stand. The supply of air or oxygen from the pipeline or cylinder enters the cabinet on the left hand side via a standard Schrader connector and hose. The outlet to the suit (or tourniquet) is in the centre of the cabinet at the front, accepting 4 mm internal diameter tubing. The tubing connecting to the suit has been adapted to include a Tycos (anaeroid type) pressure gauge using a T-piece connector. This tubing ends in a Schrader female connector, which forms the standard fitting with our suits. On the right hand side of the cabinet is the cuff valve switch, marked inflate/deflate. Just above that switch is the regulator knob which can be used to set the pressure within the suit. On the left hand side is the cuff pressure indicator, which shows red when no pressure is applied and green when the suit is inflated. The pressure gauge fitted has a lower working range than the standard orthopaedic gauge because of the smaller pressures required for suit inflation; 2–14 kPa pressure is adequate. Inside the cabinet, the pressure regulator has been set to provide an approximate flow of 20 litres/minute in order to fill the suit in a reasonable time.

The antigravity suit is fitted to the patient just prior to moving into the operating room and the patient is then placed in the sitting position. When inflation is required, the regulation control knob is rotated clockwise to the range of pressure required, as indicated on the pressure gauge; e.g. 8 kPa (60 mmHg). The cuff valve is set to inflate and the regulator knob is then adjusted to achieve the required suit pressure read from the Tycos gauge. The pressure that is normally used for these cases is 8 kPa (60 mmHg) and inflation of the suit usually takes 30 seconds.

Deflation of the suit is achieved by moving the inflation/deflation switch into the deflation position and turning the regulator knob anticlockwise.

Discussion

Neurosurgery performed in the sitting position may result in both hypotension and air embolism. The hypotension may be controlled by leg bandaging, although the effect my be variable,[2–4] or, alternatively, by the administration of large volumes of intravenous fluids with or without vasopressors.[6] The risk of air embolism arises because of subatmospheric venous pressure in the operation area and is best avoided by preventive methods, which involve raising the venous pressure. Manual neck compression may be used, although two anaesthetists are usually required as one may spend time under the towels. Recent reports have demonstrated an inflatable neck collar as an alternative.[13,14] Inflation of the collar at the times when there is greatest risk of an air embolism causes a rise in jugular venous pressure. This techniqe, however, is not effective in the prevention of hypotension. Venous pressure may be increased by positive end expiratory pressure (PEEP) or a form of expiratory resistance; up to 1.0 kPa may also be helpful in reducing the incidence of air embolism.[12,15]

This device has now been in use in the unit at the National Hospital for some time, with satisfactory results. It is very portable, allowing for movement between theatres, or may be easily fixed to an infusion stand or anaesthetic machine. It is extremely easy to use and very flexible in the pressure range of 2–14 kPa if requirements vary.

Availability

Our model was obtained through the manufacturers, Schuco International, London Ltd of Halliwick Court Place, Woodhouse Road, London N12.

References

1. Albin MS, Babinski M, Maroon JC, Jannetta PJ. Anaesthetic management of posterior fossa surgery in the sitting position. *Acta Anaesthesiologica Scandinavica* 1976; **20**: 117–28.
2. Albin MS, Jannetta PJ, Maroon JC, Tung A, Millen JE. Anesthesia in the sitting position, In: *IV European Congress of Anaesthesiology*, Madrid. Amsterdam: Excerpta Medica, 1974: 775–8.
3. Dalrymple DG, MacGowan SW, MacLeod GF. Cardiorespiratory effects of the sitting position in neurosurgery. *British Journal of Anaesthesia* 1979; **51**: 1079–81.
4. Geevarghese KP. Anesthetic management of patients undergoing surgery for posterior fossa lesions. *International Anesthesiology Clinics* 1977; **15**: 165–94.
5. Campkin TV. Posture and ventilation during

posterior fossa and cervical operations. *British Journal of Anaesthesia* 1981; **53:** 881–3.

6. Freuchen IP. The use of an antigravity suit in neurosurgery. *Acta Anaesthesiologica Scandinavica* 1959; **3:** 17–23.
7. Gardner WJ, Dohn DF. The antigravity suit (G-suit) in surgery. *Journal of the American Medical Association* 1956; **162:** 274–6.
8. Eich RH, Smulyan H, Chaffee WR. Hemodynamic response to G-suit inflation with and without ganglionic blockade. *Aerospace Medicine* 1966; **37:** 247–50.
9. Auer L. Anti-Gravitationsanzug gegen akuten Blutdruckabfall bei Operationen in sitzender Lagerung. *Acta Neurochirurgica* (Wien) 1976; **32:** 131–7.
10. Seiker HO, Burnum JB, Hickam JB, Penrod KE. Treatment of postural hypotension with a counterpressure garment. *American Journal of Medicine* 1955; **19:** 152–3.
11. Gray S 3rd, Shaver J, Kroetz FW, Leonard IJ. Acute and prolonged effects of G-suit inflation on cardiovascular dynamics. *Aerospace Medicine* 1969; **40:** 40–3.
12. Hewer AJH, Logue V. Methods of increasing the safety of neuroanaesthesia in the sitting position. *Anaesthesia* 1962; **17:** 476–81.
13. Sale JP. Prevention of air embolism during sitting neurosurgery. (The use of an inflatable neck tourniquet.) *Anaesthesia* 1984; **39:** 795–9.
14. Pfitzner J, McLean AG. Controlled neck compression in neurosurgery. *Anaesthesia* 1985; **40:** 624–9.
15. Lee DS, Lichtmann MW, Weintraub HD. Effect of PEEP on air embolism during sitting neurosurgical procedures. *Anesthesia and Analgesia* 1981; **60:** 262.

Anaesthesia, 1986, Volume 41, pages 198–204

APPARATUS

An evaluation of the Datex Normac anaesthetic agent monitor

A. D. COLQUHOUN, W. M. GRAY AND A. J. ASBURY

Summary

A new monitor for volatile anaesthetics, the Datex Normac, was assessed in the laboratory and operating theatre. The instrument had a warm up time of 90 minutes from cold, but only 5 minutes from standby. Zero drift was less than 0.01% over 7 hours, and repeated measurements of gain showed a coefficient of variation of less than 1%. However, gain drift of 6% occurred when the instrument was switched off between periods of use. Signal noise was less than 0.02 vol % on a new instrument, but was about six times greater on an instrument that had been in use for a year. The response time of 550 ms is short enough to allow breath by breath monitoring. When the instrument was calibrated on the enflurane setting, measurements made on the enflurane, halothane and isoflurane settings were accurate to within 6% of the reading. This is satisfactory for clinical purposes, but not for more demanding applications. Calibration canisters are available, and two that we tested were accurate to better than 0.1 vol %. Nitrous oxide, carbon dioxide and water vapour have very small effects on the monitor. The instrument provided trouble-free monitoring in theatre.

Key words

Anaesthetics, volatile.
Measurement techniques; infrared.

In recent years several instruments for monitoring the concentrations of volatile anaesthetic agents in breathing systems have been introduced. One of the earliest,[1] which operates on the principle of ultraviolet absorption, is only suitable for monitoring halothane. A later instrument, the Emma, is intended to monitor any one of halothane, enflurane, isoflurane, trichloroethylene or methoxyflurane.[2,3] However, this instrument, which uses a piezo-electric quartz crystal as a detector, is sensitive to water vapour, and responds too slowly to allow breath by breath monitoring of vapour concentrations.[2,3]

Datex (Helsinki, Finland)* have recently introduced the Normac monitor, an infrared absorption instrument designed to monitor halothane, enflurane, isoflurane and methoxyflurane. This instrument is claimed to be free from interference from water vapour and also to have a sufficiently rapid response time (600 ms) to allow breath by breath monitoring.

This paper presents the results of a laboratory and clinical assessment of the Normac.

*UK Supplier: Vickers Medical, Priestley Road, Basingstoke, Hampshire.

A.D. Colquhoun, MB, ChB, MRCGP, DRCOG, Department of Anaesthesia, Western Infirmary, Glasgow G11 6NT, W.M. Gray, BSc, PhD, West of Scotland Health Boards, Department of Clinical Physics and Bio-Engineering, 11 West Graham Street, Glasgow G4 9LF, A.J. Asbury, MB, ChB, FFARCS, PhD, University Department of Anaesthesia, Western Infirmary, Glasgow G11 6NT.
Correspondence should be addressed to Dr A.J. Asbury please.

0003–2409/86/020198 + 07 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Description of instrument

The Normac is a compact, mains powered instrument with dimensions 30 × 13.5 × 25 cm and weighing 8 kg. It is connected to the breathing system by fine bore tubing and a T-piece connector. The anaesthetic mixture is sampled continuously at approximately 200 ml/minute and the sampled gas, which is not degraded by the measurement process, can be returned to the breathing system.

The gas flow and optical paths are illustrated in Fig. 1. The gas passes a port, through which water is removed, and then flows into the measuring chamber. The volume of this chamber is small in order to allow a rapid response. The radiation from the infrared lamp is split into two beams, one going through the measuring chamber and the other through a sealed reference chamber containing air. The beams then pass through a filter which selects a small region of the spectrum, centred at 3.3 μm, in which the volatile agents have an absorption peak, and then pass to a solid state detector. The filter is mounted on a rotating disc which also generates additional reference signals, used to ensure instrument stability. The ratio of the responses of the transducer to the beams depends on the individual volatile agent and its concentration in the measuring chamber. The responses are linearised and further processed to give a signal which is displayed on an analogue meter, with scale graduated up to 5 vol% in 0.1 vol% subdivisions. A button on the front panel allows either continuous or peak concentrations to be displayed.

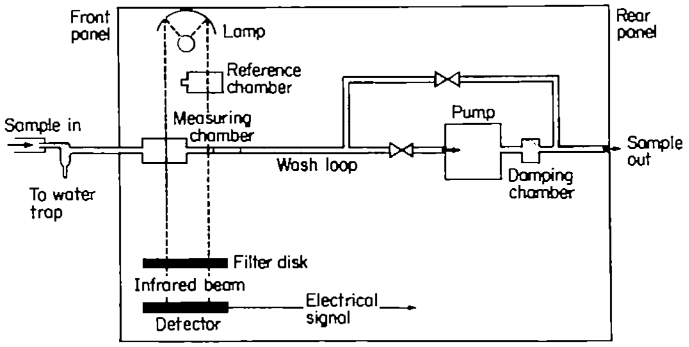


Fig. 1. Operating principle of the Normac.

The different volatile agents absorb infrared radiation to different extents so a different amplification has to be selected for each agent. Whereas the absorption by isoflurane is slightly greater than that by the same concentration of enflurane, halothane produces considerably less absorption, with the result that the amplification required is about five times greater than that for enflurane. The appropriate circuitry is selected by push switches on the front panel.

For meaningful results, only one volatile agent should be present in the sampled gas. The manufacturers claim that interference from nitrous oxide, carbon dioxide and water vapour, all of which absorb infrared radiation at certain wavelengths, is minimal. However, they warn that alcohol vapour affects the accuracy of the readings. The instrument has external zero and gain controls. A canister containing a halocarbon mixture equivalent to a stated concentration of enflurane is provided for calibration.

There is an audible alarm to indicate when the vapour concentration is outside adjustable low and high limits. A 5-pole DIN socket at the rear of the instrument provides an analogue output signal proportional to anaesthetic agent concentration, and also provides appropriate signals for a remote alarm. The instrument is accompanied by a comprehensive and clearly written instruction manual.

Methods

Most of the laboratory evaluation was carried out with an instrument loaned by the suppliers. The clinical assessment and certain laboratory checks were done with a second instrument, which had been in clinical use for about one year. Unless indicated otherwise, the tests described below were carried out on the first instrument.

Laboratory assessment

The instrument's performance was assessed for halothane (Fluothane, ICI), enflurane (Ethrane, Abbott) and isoflurane (Aerrane, Ohio). Methoxyflurane was not used, since it has been withdrawn from sale in the U.K. Five litres/minute of oxygen were supplied by a standard Boyles machine, with the volatile agent added from Cyprane Tec 3 vaporizers with Selectatec fittings. Samples were taken from a cannula inserted into the tubing carrying the gas stream.

To permit more accurate readings than were possible on the internal analogue meter, a digital voltmeter (Weston model 6400) was connected to the DIN socket. For continuous recordings the output signal was displayed either on a potentiometric recorder (Curken or Linseis) or a high speed UV recorder (SE Labs model 3006).

A 50 ml gas-tight Hamilton syringe, fitted with a two-way Hamilton valve, was used to collect samples for chromatography. The samples were analysed in duplicate, using a Pye Unicam PU4500 gas chromatograph (GC), fitted with a 2-metre long, 4-mm internal diameter glass column packed with 80–100 mesh Chromosorb WHP coated with 10% silicone OV101. The oven temperature was 200°C and the carrier gas was oxygen-free nitrogen at a flow of 40 ml/minute. A flame ionisation detector, operating at 250°C, was used, and the output signal fed to a Hewlett Packard HP 3390A reporting integrator; peak area was used as a measure of concentration. The samples were introduced to the carrier gas stream by means of a Valco gas sampling valve fitted with a 100 μl loop. The retention time was 0.6 minutes for all three volatile agents. The gas chromatograph was calibrated using standard mixtures prepared by a static dilution method with a relative standard error of less than 0.5%.[4]

The following tests were carried out in a well ventilated laboratory equipped with a scavenging system.

Earth leakage was tested to BS5724 requirements,[5] using a Rigel 233 electrical safety tester.

Warm-up time was measured by switching the instrument to 'measure', either from 'off' or from 'standby', and recording the output voltage on a potentiometric recorder, with the instrument sampling room air.

Zero drift was measured from a 7-hour tracing from a potentiometric recorder, obtained on the enflurane setting with the instrument sampling room air.

Noise was estimated from potentiometric recorder tracings, on the enflurane and halothane settings, for room air sampling. This test was carried out on both instruments, under similar environmental conditions.

Short term gain drift was estimated by repetition of the following cycle. The instrument was set to zero on oxygen, then the Enfluratec was set to 1% and the GC and Normac responses obtained; the vaporizer was then switched off. The cycle was carried out at 5-minute intervals for 45 minutes and also at 30-minute intervals for 4.5 hours. For each set of ten measurements, the instrument's response was normalised to 1% (to take account of drift in the vaporizer output), and the coefficient of variation calculated).

Long term gain drift was assessed using the one-year-old instrument. It was calibrated as described above and its response to 1% enflurane measured against the GC one week later. The instrument had been switched off for most of the intervening period.

Response time was estimated by quickly removing the sampling connector from a 1% enflurane mixture and measuring the time for the signal to change from 90% to 10% of the initial level, on the UV recorder tracing.

Linearity and amplification were checked by calibrating the Normac against the GC, using a 1% enflurane mixture, and then making a series of measurements on the GC and Normac at different enflurane concentrations. Measurements were made with increasing and decreasing concentrations. The study was repeated using isoflurane and halothane, without changing the initial calibration setting. An additional set of enflurane measurements was made with a carrier flow of 1 litre/minute of oxygen. In each case, linear regression analysis was carried out, with GC reading as independent variable (x) and Normac reading as dependent variable (y). The values of a and b in the expression $y = ax + b$ were estimated.

Accuracy of calibration canisters. Two canisters were checked (one new and one nearly exhausted) using the Normac. The maximum stable reading was recorded and the actual concentration obtained from the enflurane calibration graph.

Interference from nitrous oxide, carbon dioxide and water vapour. The effects of differing concentrations of nitrous oxide (20, 40, 60, 80, 100%), carbon dioxide (5, 9, 40, 100%) and oxygen saturated with water vapour at 37°C on the Normac's zero reading were recorded.

Clinical assessment

An instrument which had been in clinical use for one year without maintenance was assessed in a variety of general anaesthetic procedures. A continuous record was obtained with a potentiometric recorder.

Results

Laboratory assessment

Earth leakage. The instrument passed the earth leakage requirements of BS5724, both for normal operation and under a single fault condition (open supply).

Warm-up time. The warm-up time from cold was approximately 90 minutes (three times the manufacturer's specified value), but this was reduced to 5 minutes if the unit was left in standby mode.

Zero drift. The zero drift (maximum reading–minimum reading) over the period of 7 hours was 0.002 vol% on the enflurane setting.

Noise. For the instrument on loan from the suppliers, the peak-to-peak noise amplitude was 0.003% for enflurane and 0.015% for halothane. For the one-year-old instrument, the corresponding readings were 0.02% and 0.1%.

Short term gain drift. The coefficients of variation for 5 and 30 minute sampling were 0.55% and 0.15% respectively.

Long term gain drift. One week after calibration, the instrument read high, by 6% of the concentration.

Response time. The mean response time was 554 ms (SEM 14 ms) which is in close agreement with the manufacturers specification of 600 ms.

Linearity and amplification (Figs 2–4). There was a high correlation between the values recorded by the GC and the Normac, with all the correlation coefficients in excess of 0.99. When measuring halothane, the instrument consistently over-read, whereas with enflurane and isoflurane it under-read at low concentrations and over-read at high concentrations. The greatest error was 6% of the reading. Data for enflurane at 1 litre/minute were similar to those for enflurane at 5 litres/minute. No hysteresis was observed.

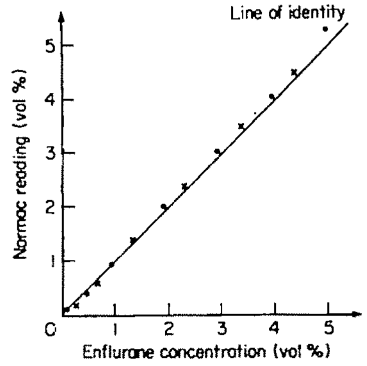


Fig. 2. Enflurane calibration. ●, Ascending; x, descending; $n = 13$; $a = 1.05$ (SE 0.01); $b = -0.04\%$ (SE 0.02%).

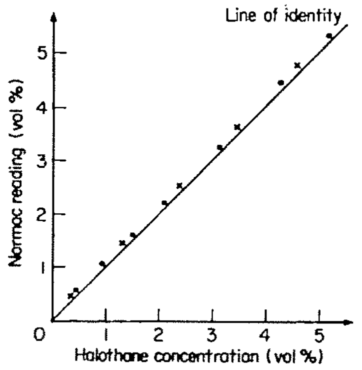


Fig. 3. Halothane calibration. ●, Ascending; x, descending; $n = 14$; $a = 1.02$ (SE 0.01); $b = 0.02\%$ (SE = 0.02%).

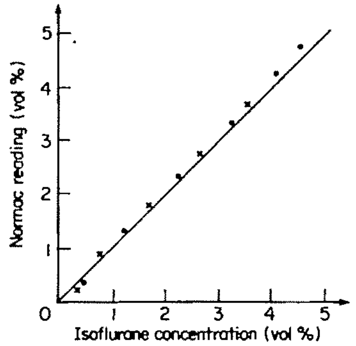


Fig. 4. Isoflurane calibration. ●, Ascending; x, descending; $n = 12$; $a = 1.05$ (SE 0.01); $b = -0.03\%$ (SE 0.01%).

Accuracy of calibration canisters. The canister with a stated enflurane equivalent of 2.66%

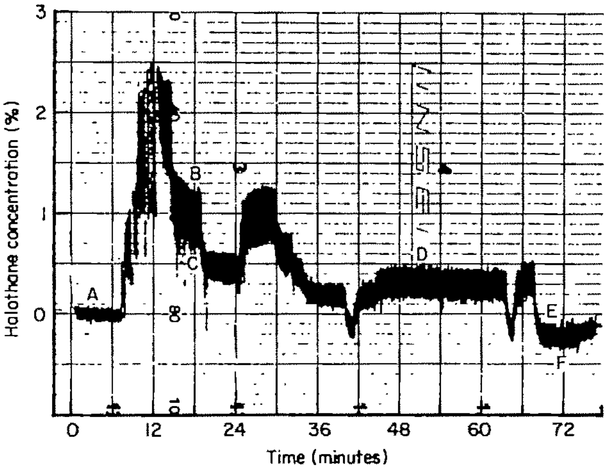


Fig. 5. Halothane concentration measured in Mapleson A system; sampling from oral end of the tracheal tube; fresh gas flow 4 litres/minute N_2O, 2 litres/minute O_2. (A), No halothane in system; (B), inspiratory halothane concentration; (C), expiratory halothane concentration; (D), uneven tracing caused by signal noise (compare Fig. 6,D); (E), expiratory halothane concentration with vaporizer off; (F), inspiratory halothane concentration with vaporizer off (note zero drift).

measured 2.72% (SEM 0.02%) whereas the canister marked 2.85% measured 2.85% (SEM 0.02%).

Interference from nitrous oxide, carbon dioxide and water vapour. With 100% nitrous oxide, the maximum effect was observed when measuring halothane and amounted to −0.15%; the reading was −0.03% with enflurane and isoflurane. Carbon dioxide and oxygen saturated with water vapour at 37°C gave no reading on any setting.

Clinical assessment

The equipment was easy to set up and provided clinically useful information in a variety of anaesthetic procedures. Figures 5–7 are typical tracings, illustrating a number of points. The noise on the halothane setting (Fig. 5,A) is considerably greater than that on the isoflurane setting (Fig. 6,A). Breath by breath measurements are possible, allowing useful monitoring of end tidal concentrations (Fig. 7b). In Figure 5, the final

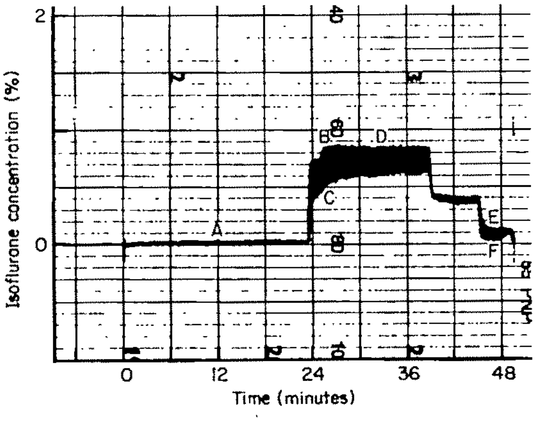


Fig. 6. Isoflurane concentration at oral end of tracheal tube for a patient ventilated with 3.5 litres/minute N_2O and 3.5 litres/minute O_2 by a Manley Pulmovent. (A), No isoflurane in system; (B), inspiratory isoflurane concentration; (C), expiratory isoflurane concentration; (D), smoother tracing compared with Fig. 5,D: (E), expiratory isoflurane concentration with vaporizer off; (F), inspiratory isoflurane concentration with vaporizer off.

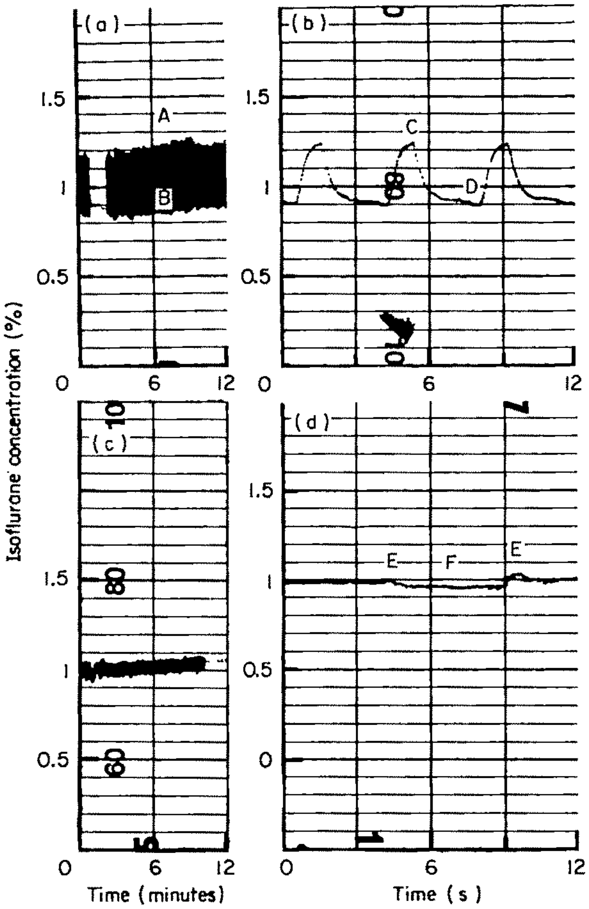


Fig. 7. Isoflurane concentration in a low flow circle system with the patient breathing spontaneously. A fresh gas flow of 500 ml/minute N_2O and 500 ml/minute O_2 was used, with CO_2 absorber in the system throughout, and vaporizer situated outside the circle, (a) Sampling at tracheal tube: (A), inspiratory concentration, (B) expiratory concentration; (b), sampling at tracheal tube: (C), peak inspiratory concentration, (D), trough expiratory concentration; (c), sampling from inspiratory limb of the breathing system; (d), sampling from inspiratory limb of the breathing system: (E), inspiration, (F), expiration.

level of halothane (E) was about 0.2% below the starting zero level (A); this was probably a result of a warm-up time of only 20 minutes instead of the 90 minutes suggested by the laboratory data.

Discussion

We found the Normac to be well designed, reliable and easy to use. It is virtually unaffected by water vapour, carbon dioxide or nitrous oxide, and its response time is sufficiently short to allow breath by breath monitoring.

The laboratory assessment shows that the instrument is sufficiently accurate for clinical purposes. The relative electronic gains for the different agents are such that the instrument can be used for all three agents on the basis of the enflurane calibration. However, for each agent, the calibration curve shows some departure from the line of identity, and this discrepancy is great enough to preclude the use of the monitor for applications where an accuracy of better than 5% is required. It is possible that this aspect could be improved by internal adjustments to the electronic circuitry.

The instrument is sufficiently accurate for clinical purposes. The relative electronic gains for the different agents are such that the instrument can be used for all three agents on the basis of the enflurane calibration. However, for each agent,

the calibration curve shows some departure from the line of identity, and this discrepancy is great enough to preclude the use of the monitor for applications where an accuracy of better than 5% is required. It is possible that this aspect could be improved by internal adjustments to the electronic circuitry.

For greatest accuracy in clinical use the instrument should be calibrated if it has been switched off since previous calibration. The enflurane equivalent canisters that we tested were accurate, and these should provide better calibration than an anaesthetic vaporizer, whose output may change over a period of time, even though it may be thermally compensated. However, this method makes the user dependent upon the availability and accuracy of the canisters to keep the unit in active use.

There are a number of minor limitations to the clinical use of the instrument. The long warm-up time from 'off' leads us to suggest that the unit should be left on standby when not in use or switched on first thing in the morning, while normal theatre preparations are made. The instrument is least precise in determining concentrations of halothane, the most common volatile anaesthetic. It will not give a reliable reading when two volatile agents are present. In view of the relative electronic gains, this problem is likely to be greatest when changing from isoflurane to halothane. Finally, ethanol vapour in the sampled gas also causes a spurious reading.

It is important to have the instrument serviced regularly to keep the optical system clean. The second instrument that we examined had been in service for over a year, with no maintenance, and the noise on the output signal was about five times greater than with the instrument loaned by the suppliers, amounting to 0.2 vol% on the halothane setting.

Acknowledgments

The authors thank Vickers Medical and Dr C.S. Cairns for the loan of the Normacs and Mrs J. Buttar for skilfully typing this manuscript.

References

1. Diprose KV, Epstein HG, Redman LR. An improved ultra-violet halothane meter. *British Journal of Anaesthesia* 1980; **52**: 1155–60.
2. Kay B, Cohen AT, Wheeler MF. A laboratory investigation of a multigas monitor for anaesthesia (Emma). *Anaesthesia* 1982; **37**: 446–50.
3. Hayes JK, Westenskow DR, Jordan WS. Monitoring anesthetic vapor concentrations using a piezoelectric detector: evaluation of the Engstrom Emma. *Anesthesiology* 1983; **59**: 435–9.
4. Gray WM. A static calibration method for the gas chromatographic determination of per cent concentrations of volatile anaesthetics. *British Journal of Anaesthesia* (in press).
5. British Standards Institution. *British Standard 5724. Specification for safety of medical electrical equipment. Part 1. General requirements* London: BSI, 1979.

Anaesthesia, 1986, Volume 41, pages 205–207

Forum

Local complications following intravenous benzodiazepines in the dorsum of the hand. A comparison between midazolam and Diazemuls in sedation for dentistry

J. J. Margary, MB, BS, FFARCS, Senior Registrar, Department of Anaesthetics, St George's Hospital, Blackshaw Road, London SW17 0QT, N.L. Rosenbaum, BDS, Senior Lecturer in Oral Surgery, The United Medical and Dental Schools of Guy's and St. Thomas's Hospital, London Bridge, SE1 QRT, M. Partridge, FDSRCS, Lecturer in Oral Surgery, King's College Hospital, Denmark Hill, London SE5 9RS, S. Shankar, FRCS, FDS, FFD, Senior Registrar in Oral Surgery, The Royal Dental Hospital of London School of Dental Surgery, Leicester Square, London WC2H 7LL.

Summary

Two hundred patients requiring sedation for minor oral surgery were randomly allocated to receive either midazolam or diazepam as Diazemuls intravenously through a 23-gauge indwelling needle in the dorsum of the hand. The site of injection was inspected at 7 days and 14 days post injection and assessed for pain, tenderness, redness, induration, painless thrombosis, and thrombophlebitis. The mean dose administered was 0.119 mg/kg of midazolam and 0.298 mg/kg of Diazemuls. At 7 days there was no significant difference in venous complications. At the 14 day follow up, the midazolam group had a significantly greater incidence of tenderness and redness ($p < 0.001$ and $p < 0.05$ respectively using Chi squared test). The incidence of thrombophlebitis in the midazolam group was 2% at 7 days and 1% at 14 days, the corresponding figures in those given Diazemuls being none and 1% respectively. We conclude that the dorsum of the hand is a satisfactory site of injection for administration of these drugs. The higher incidence of minor complications at 14 days following midazolam was offset by its more reliable amnesic properties.

Key words

Hypnotics, benzodiazepines; midazolam, diazepam (Diazemuls).
Complications; thrombosis.

Diazepam and midazolam have both been shown to be suitable agents for intravenous sedation in dentistry. The benzodiazepines, however, are relatively slow in onset when given in this way and patient response can be very variable. Hence, these sedatives should be titrated against patient response via a stable intravenous access. The dorsum of the hand is a stable and convenient site for inserting indwelling intravenous needles, but the veins are small and therefore likely to be particularly sensitive to injections of irritant substances.

We compared the local venous sequelae following sedation using the water soluble benzodiazepine, midazolam 5 mg/ml (Hypnovel), and diazepam in soya bean oil emulsion 5 mg/ml (Diazemuls), when injected into the dorsum of the hand using a 23-gauge winged needle.

Methods

Two hundred adult patients attending the outpatient dental department or dental practice for minor oral surgical procedures and in whom sedation was necessary, were included in the study, which was approved by the local Ethical Committee. Informed consent was obtained from the patients, who were randomly allocated to receive midazolam or Diazemuls.

A 23-gauge indwelling needle was inserted into a vein on the dorsum of the hand. If venepuncture was unsuccessful, the other hand was used. If venepuncture failed in both hands, the patient was excluded from the trial. The needle remained *in situ* during the procedure and was removed on completion of the procedure. Firm pressure was applied to the venepuncture site using a swab and adhesive tape. The skin

---

Correspondence should be addressed to N. L. Rosenbaum, Department of Oral Surgery, The United Medical and Dental Schools of Guy's and St. Thomas's Hospitals, London Bridge, London, SE1 9RT.

0003–2409/86/020205 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

was always swabbed with isopropyl alcohol and allowed to dry before venepuncture. No other drugs were given through the needle, and the blood pressure was always taken in the opposite arm. Diazemuls was given at a rate of 2 mg/15 seconds until 0.2 mg/kg had been administered, and midazolam 0.07 mg/kg at a rate of 1 mg/20 seconds. Additional increments were given as required to achieve satisfactory sedation. Local anaesthetic dental blocks were injected 2 minutes after completion of the sedative injection. The volume required to fill the dead-space of the needle was not considered as part of the administered dose.

At the end of the procedure, the operator graded the quality of sedation as 1, 2, or 3 corresponding to good, fair, or poor. In the Diazemuls group, the needles remained *in situ* for a mean of 29.7 minutes (SD 9.5), and in the midazolam group for a mean of 24.9 minutes (SD 10.5). All patients were seen again at 7 and 14 days post treatment and the site of intravenous injection was examined. This was assessed at both follow-ups for pain, tenderness, redness, induration, painless thrombosis, and thrombophlebitis. Cases of thrombophlebitis were followed up until symptoms had waned.

Results

Table 1 details the sex, and the mean age, weight, and dose of sedative. There was no significant difference between the patients in the two groups. The mean quality of sedation score was 1.18 for the midazolam group and 1.50 for Diazemuls. No procedure had to be abandoned as a result of poor sedation.

Table 1. Patient data

	Midazolam	Diazemuls
Number	100 (M32/F68)	100 (M31/F69)
Mean weight (kg)	60.69	61.57
Mean age (years)	36.65	34.17
Mean total dose (mg/kg)	0.119	0.298
Mean quality of sedation	1.18	1.50

The complications found at the 7 and 14 day examinations of the injection site are shown in Table 2. There was no significant difference in venous sequelae between the two groups at 7 days (Chi squared test). At the 14 day post treatment follow-up, the midazolam group showed a significantly greater incidence of tenderness ($p < 0.001$) and redness ($p < 0.05$). The incidence of thrombophlebitis was not significantly different. One patient in each group had thrombophlebitis extending up the forearm at 14 days. In both of these patients, the tenderness over the vein had resolved by 4 weeks, although the vein was still indurated.

Discussion

A controlled comparative study of the venous complications following intravenous injection of midazolam or Diazemuls in the dorsum of the hand has not been previously reported. Previous studies[1,2] have demonstrated the low incidence of venous complications when Diazemuls is injected at this site. It has also been demonstrated that midazolam also causes a low incidence of local venous complications[3] when injected at various sites in the arm, although it has been suspected of causing late thrombophlebitis. This study has compared the complications following administration of each of these two agents when injected only into the veins of the dorsum of the hand. Seven and 14-day follow-ups were made to detect any delayed venous complications.

We believe that a continuous intravenous access should be used when administering benzodiazepines for sedation because of their relatively slow onset of action and the great variability of patient response. This allows careful titration of the sedative to achieve the desired depth of sedation. Midazolam, as confirmed in this study, produces a more profound sedation than diazepam, and therefore should be more carefully titrated to prevent accidental over-sedation.[4]

For this reason, the veins on the dorsum of the hand were chosen, on account of their ease of cannulation, accessibility, and the stability of the site for an indwelling needle. We also used winged indwelling needles since they are simple to insert into these veins. The disadvantage of the veins on the dorsum of the hand are that the veins are small and carry a relatively small blood flow compared with more proximal veins. Hence, they are more susceptible to irritant injections.

In this study, the incidence of major sequelae (thrombosis and thrombophlebitis) was low and not sig-

Table 2. Incidence of venous sequelae

	7 days		14 days	
Observation	Midazolam	Diazemuls	Midazolam	Diazemuls
Pain	2	1	1	1
Tenderness	18	12	23*	3*
Redness	23	18	9†	1†
Induration	6	5	6	2
Painless thrombosis	3	3	6	2
Thrombophlebitis	2	0	1	1
None	67	79	71†	93†

*$p < 0.001$; †$p < 0.05$; (χ^2 test).

nificantly different. However, a significantly greater incidence of tenderness and redness following midazolam was seen at 14 days. Midazolam hydrochloride is presented in an aqueous solution with a pH of less than 4; this low pH could account for the greater incidence of venous sequelae.

We conclude that both of these agents proved to be satisfactory agents for sedation in dentistry. Although midazolam had a higher incidence of minor complications when injected in the dorsum of the hand, it should be remembered that even intravenous injection of isotonic saline causes an incidence of venous sequelae.[2]

Acknowledgments

We would like to thank Professor D. Poswillo and Professor J. Sowray for their cooperation. We also thank Kabivitrum Ltd. and Roche Products Ltd. for supplying the drugs Diazemuls and Hypnovel, respectively.

References

1. Rosenbaum NL. A new formulation of diazepam for intravenous sedation in dentistry. *British Dental Journal* 1982; **153:** 192–3.
2. Kawar P, Dundee JW. Frequency of pain on injection and venous sequelae following I.V. administration of certain anaesthetics and sedatives. *British Journal of Anaesthesia* 1982; **54:** 935–9.
3. Al-Khudhairi D, Whitwam JG, McCloy RF. Midazolam and diazepam for gastroscopy. *Anaesthesia* 1982; **37:** 1002–6.
4. Committee on safety of medicines. Midazolam (Hypnovel)—respiratory depression and hypotension. *Current Problems* 14, February 1985.

Anaesthesia, 1986, Volume 41, pages 208–226

Correspondence

Generic names 209
E.T. Matthews, FFARCS
Indications for blood microfiltration 210
K. Linko, MD
M. Clare Derrington, FFARCS 210
Buprenorphine–naloxone synergism: evidence for dual system hypothesis of pain perception 211
M.A. Gillman, BDS, MSc, BSc, and F.J. Lichtigfeld, MB, BCh, F.F. Psych(SA)
Etomidate and Cushing's syndrome 211
J. Costa, MD, D. Ramos, MD, S. Massada, MD, D. Carvalho, MD, and D. Pignatelli, MD
Loss of consciousness after caudal injection 212
P.A.J. Hardy, BSc, FFARCS
Are armoured tracheal tubes really necessary for neuroanaesthesia? 213
P.J. Wright, FFARCS
Use of atracurium and labetalol in a patient with phaeochromocytoma 213
A. Sheikh, FFARCS
Pain on injection with droperidol and prevention of pain with etomidate 214
J.C. Coghill, FFARCS
Another hazard of heated water humidifiers 215
H.S. Smith, FFARCS and R. Allen, ONC (Mech. Eng.)
Induction agent sensitivity and ophthalmoplegia plus 216
R.H. James, FFARCS
A modification of the linear analogue 217
J.P. Jayasuriya, FFARCS
Pass rates in the final FFARCS examination 217
J. Norman, PhD, FFARCS
A computer-generated guide for paediatric anaesthesia 218
E.C. Bloch, FFARCS
Modification of laryngoscope for nasogastric intubation 218
Fiona McWhinnie, FFARCS
A mistaken case of hypersensitivity to a local anaesthetic 219
Y. Mehta, MD, FFARCS and M.C. Luxton, FFARCS
Ulnar nerve stimulation in the thick arm 220
D.A. Cozanitis, MD
Failure of injection during attempted spinal anaesthesia 220
N.C.T. Wilton, MRCP, FFARCS and T.S. Brown, MB, BS, DA
Tracheal administration of drugs 221
M.B. Taylor, FFARCS and D.A. Zideman, BSc, FFARCS
Topical lignocaine after tonsillectomy in children 222
Alison Williams, FFARCS and A. Hamilton, FFARCS
Labelling of drugs 222
M.J.A. Parr, MB, BS
A tunnelling technique for central venous catheters 224
N.M. Woodhall, FFARCS and D.R. Redman, FFARCS
Hazard from the oxygen flush control 222
N. Puttick, FFARCS
Diluting suxamethonium 225
R.W.D. Nickalls, BSc, FFARCS
Rough and Ready 225
K. Birkenshaw, FFARCS
Resuscitative skills 226
J.A. Lee, FFARCS

All correspondence should be addressed to Dr J.N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

Letters must be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters contained in 'Notice to Contributors' to *Anaesthesia* printed at the back of each issue. The degrees and diplomas of each author must be given in a covering letter personally signed by all the authors.

Correspondence presented in any other style or format may be the subject of considerable delay and may be returned to the author for revision.

Generic names

The convention that only generic names of drugs are used in scientific papers is long established. Attempts to challenge the validity of this practice have met with strong editorial resistance.[1] Conforming to this convention may conceal information which is scientifically and therapeutically relevant.

In 1978 a paper described the suppression of response to surgery when fentanyl 50 μg/kg was given before surgery.[2] A second paper from the same hospital, published in 1984, described the failure of fentanyl 50 μg/kg, given 60 minutes after surgery began, to suppress the responses to surgery.[3] A 70-kg patient in 1978 would have received not only 3500 μg fentanyl but also 35 000 μg methyl hydrobenzoate and 3500 μg propyl hydrobenzoate. The formulation changed in 1980 and a similar patient in 1984 would have received fentanyl alone.

The convention of generic name only meant the the presence of large amounts of other drugs was unreported. Nathan and Sears stressed that the presence of the hydroxybenzoates must be taken into account in both experimental and therapeutic situations,[4] so, since these drugs can block conduction in nerves, it would be proper to take their effects into account. There are no previous reports of the effects of such large amounts of the hydroxybenzoates given intravenously in man.

The formulations of such basic drugs as morphine may also differ significantly. Several studies of high dose morphine for cardiac surgery have been published. Variations in the formulation used in different centres may invalidate comparisons. The Macarthy preparation (UK) contains chlorocresol 2 mg and metabisulphate 1 mg, whereas that of Lilly (USA) contains chlorobutanol 5 mg and sodium bisulphate 1 mg. The chlorobutanol in the American preparation is a chloral hydrate derivative with hypnotic and anti-emetic properties. It may be a useful supplement to the anaesthesia. Chlorocresol is more likely to have adverse therapeutic effects.

Other ampoules we use contain a wide and variable variety of additives. They include anti-oxidants, bacteriostats, diluents, emulsifiers, fungistats, stabilisers, solvents, suspending agents and tonicity and pH adjusters. Information about these additives, classified as inactive ingredients, does not *have* to appear on the label and may not be found by reference to the British Pharmacopeia (BP), the British Pharmacopeia Codex, Martindale's Extra Pharmacopoeia, the British National Formulary, The Monthly Index of Medical Specialties, or the Data Sheet. The information is only available from the manufacturer. Some manufacturers, such as Janssen, provide it readily. May and Baker provide the information but forbid its publication. Roche would not release the information but gave a confidential list to the hospital pharmacist because they wish to control the circulation of such information for commercial reasons, despite evidence about bioavailability of diazepam.[5]

In the United States of America, the Food and Drug Administration have released a list of over 700 inactive ingredients which may be included in Approved Prescription Drug Products. The list includes alcohol, absolute alcohol, denatured alcohol, and alcohol diluted. In 1982, the inadvertent use of ampoules of saline which, unknown to the clinicians, contained benzyl alcohol as a preservative caused the deaths of 15 patients. Both the United States Pharmacopeia and BP allow the inclusion of a suitable bacteriostat in the preparation of saline for injection.

The information on the Data Sheet may even be misleading because it may state what is not included, but omit that which is included in the formulation. The Data Sheet for one preparation of nitroglycerin, Nitrocine (Sanol Schwarz Pharmaceuticals Ltd.) states that it 'does not contain alcohol or potassium', but it does not state that propylene glycol is in the formulation. A case of propylene glycol intoxication due to a similar formulation of nitroglycerin has been reported.[6] The requirements of The Medicines (Data Sheet) Regulations 1972 should be amended to prevent this type of entry.

Editors should now abandon this convention and insist that, in addition to the generic name, the source (brand name) and the formulation be included in each report. This change would, in my opinion, facilitate scientifically valid comparisons of published work and contribute to therapeutic safety.

Queen Elizabeth Hospital, E.T. MATTHEWS
Edgbaston,
Birmingham, B15 2TH

References

1. EDITORIAL. Names of drugs. *British Medical Journal* 1977; **2:** 980.
2. HALL GM, YOUNG C, HOLDCROFT A, ALAGHBAND-ZADEH J. Substrate mobilisation during surgery. A comparison between halothane and fentanyl anaesthesia. *Anaesthesia* 1978; **33:** 924–30.
3. BENT JM, PATERSON JL, MASHITER K, HALL GM. Effects of high-dose fentanyl anaesthesia on the established metabolic and endocrine response to surgery. *Anaesthesia* 1984; **39:** 19–23.
4. NATHAN PW, SEARS TA. Action of methyl hydroxybenzoate on nervous conduction. *Nature* 1961; **192:** 668–9.
5. FEE JPH, DUNDEE JW, COLLIER PS, MCCLEAN E. Bioavailability of intravenous diazepam. *Lancet* 1984; **2:** 813.
6. DEMEY H, DAELEMANS R, DE BROE ME, BOSSAERT L. Propyleneglycol intoxication due to intravenous nitroglycerin. *Lancet* 1984; **1:** 1360.

Indications for blood microfiltration

The review by Dr Derrington on 'The present status of blood filtration' (*Anaesthesia* 1985; **40:** 334–47) was very interesting. Even though the subject has been reviewed before,[1] it certainly deserves re-evaluation from time to time. It is easy to agree with the writer on most points brought up in the article. However, I would like to comment on certain arguments in the summary and conclusions.

Dr Derrington concludes that the only indications for using microfilters are cardiopulmonary bypass and the preparation of granulocyte poor blood. However, aggregates (and granulocytes) can also be removed simply by a standard transfusion set filter.[2] Regardless of the filter used, blood must be stored for about one week and centrifuged prior to filtration in order to increase the particle size of the aggregates and the granulocyte harvest. Granulocyte poor blood is mainly used to reduce the number and severity of febrile transfusion reactions, while the main indication for microfilters is massive blood transfusion.

In Dr Derrington's opinion, red cell concentrates should be used instead of whole blood, even for massive transfusions. If the buffy coat is removed during the preparation of red cell concentrates, they contain very few aggregates, which makes microfiltration unnecessary. However, whole blood containing large quantities of aggregates is still widely used, especially for massive transfusions mainly because of the technical simplicity. Whether the removal of aggregates from stored blood reduces the incidence of the adult respiratory distress syndrome is unclear. Certainly micro-aggregates cannot be of any benefit to the patient.

The conclusion, with which I disagree, is that when exsanguination is a risk, microfiltration may be dangerous. The pressure drop across microfiltration devices is usually less than that caused by a regular transfusion set.[3,4] This is mainly dependent on the dimensions of the transfusion line.[5] Microfilters may become occluded by debris originating from the blood, and thus cause additional resistance to flow. However, the filtration capacity of the microfilters on the market is variable[6] and the filters with the highest capacity easily tolerate 5–7 units of stored whole blood, which is more than can be expected with standard transfusion sets. Thus, the main indication for using microfilters is rapid massive transfusion with stored whole blood. Filters do not cause any risk to the heavily bleeding patient. On the contrary, a good microfilter is an essential part of the transfusion equipment. Microfiltration of blood has been a routine in our clinic for 5 years. Several patients have now received blood transfusions exceeding 100 units of stored whole blood (max 186 units) during a single operation. This would hardly have been possible without the microfiltration device (Fenwal C2135), even though other technical details are important as well.

Department of Anaesthesia, K. Linko
Helsinki University Central Hospital,
Haartmaninkatu 4,
00290 Helsinki 29, Finland

References

1. Linko K. Does blood transfusion cause respiratory failure. *Annales Chirurgiae et Gynaecologiae* 1982; (Suppl); **71:** 37–41.
2. Linko K. Observations on the removal of microaggregates from stored blood by centrifugation and filtration through a standard 170 μm transfusion set filter. *Transfusion* 1983; **23:** 310–2.
3. Linko K. In-line blood warming and microfiltration devices I. Testing of flow and warming properties by pressure transfusion of aggregate-free blood. *Acta Anaesthiologica Scandinavica* 1979; **23:** 40–5.
4. Linko K. In-line blood warming and microfiltration devices II. Influence of blood temperature on flow rate and hemolysis during pressure transfusion through micro-filters and transfusion sets. *Acta Anaesthesiologica Scandinavica* 1979; **23:** 46–50.
5. Palosaari S, Linko K. Flow of blood in transfusion systems. *Biorheology* 1980; **17:** 385–90.
6. Linko K. An *in vitro* comparison of six microaggregate blood filters. *Acta Anaesthesiologica Scandinavica* 1979; **23:** 603–12.

A reply

Dr Linko's comments are most useful but, in answer to his criticism about the expected use of red cell concentrates, it was not my intention to suggest that red cell concentrates alone should be used in massive transfusion. Red cells, plasma, platelets and clotting factors should be used together to treat massive blood loss.

The relationship between micro-aggregates in stored blood and the incidence of adult respiratory distress syndrome (ARDS) is, I agree, far from proven. It is the automatic use of microfilters in the belief that they reduce the incidence of ARDS that I criticise.

The statement that the main indication for the use of microfilters is rapid massive transfusion with stored blood is more difficult to accept. The standard transfusion filter *may* block more rapidly than some microfilters but this is likely to be related to the surface area available for filtration, not the pore size. This is therefore an argument for enlargement of the filtration surface in the standard 160 μm filter, not for the use of microfilters.

The case for the use of microfilters remains at the moment, in my view, unproven.

University Department of M. Clare Derrington
Anaesthesia,
Leicester Royal Infirmary,
Leicester, LE1 5WW

Buprenorphine–naloxone synergism: evidence for dual system hypothesis of pain perception

Schmidt *et al.* in their recent paper (*Anaesthesia* 1985; **40**: 583–6) have presented data which provided very strong evidence for the synergistic effects of naloxone in combination with buprenorphine in pain relief. This finding had been previously reported by Dum and Herz, who showed that the agonist potency of higher doses of buprenorphine was increased by the concomitant administration of the opioid antagonist naltrexone. They explained this apparently paradoxical effect by suggesting that it might be due to cooperativity at the receptor.[1]

We have considered such an explanation in attempting to clarify our own findings, in which naloxone potentiated the effects of opioid agonists, i.e. analgesic nitrous oxide[2] and morphine[3] and which led us to postulate the use of pure opioid antagonists as analgesics.[4] Furthermore, as a result of this work we have proposed the dual system hypothesis of pain perception, based on the presence of both an opioid and anti-opioid system with differential sensitivities to naloxone.[2,3,5,6] Using this hypothesis it is possible to explain these paradoxical effects of pure opioid antagonists. Experimental confirmation of the presence of such an hyperalgesic anti-opioid system has been presented by Wu *et al.*, who have localised this system in the pontine-medullary region.[7]

South African Brain
Research Institute,
Suite 9, Highlands House,
173 Louis Botha Avenue, 1
Orange Grove, 2192,
Johannesburg, South Africa

M.A. Gillman
F.J. Lichtigfeld

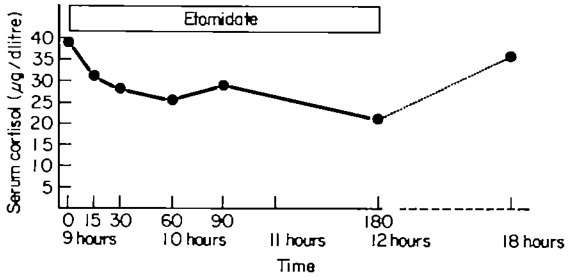
References

1. Dum JE, Herz A. *In vivo* receptor binding of the opiate partial agonist, buprenorphine, correlated with its agonistic and antagonistic actions. *British Journal of Pharmacology* 1981; **74**: 627–33.
2. Gillman MA, Kok L, Lichtigfeld FJ. Paradoxical effect of naloxone on nitrous oxide analgesia in man. *European Journal of Pharmacology* 1980; **61**: 175–7.
3. Gillman MA, Lichtigfeld FJ. A comparison of the effects of morphine sulphate and nitrous oxide analgesia on chronic pain states in man. *Journal of Neurological Sciences* 1981; **49**: 41–5.
4. Gillman MA, Lichtigfeld FJ. Intraspinal opiates and itching. A new reflex? *British Medical Journal* 1982; **284**: 1950.
5. Gillman MA, Kimmel I, Lichtigfeld FJ. The dual-system hypothesis of pain perception. *Neurological Research* 1981; **3**: 317–27.
6. Gillman MA, Lichtigfeld FJ. A pharmacological overview of opioid mechanisms mediating analgesia and hyperalgesia. *Neurological Research* (in press).
7. Wu KM, Martin WR, Kamerling SG, Wettstein JG. Possible medullary kappa hyperalgesic mechanism. 1. A new potential role for endogenous opioid peptides in pain perception. *Life Sciences* 1983; **33**: 1831–8.

Etomidate and Cushing's syndrome.

Etomidate, an imidazole-derived anaesthetic, is used for induction and maintenance of anaesthesia and, until recently, for prolonged sedation of critically ill patients. This drug may be administered either by bolus injection or continuous infusion, and is characterised by a rapid onset of action and recovery and lack of cardiovascular depression.[1]

Ledingham's letter,[2] which reported increased mortality in intensive care units associated with the use of etomidate, was followed by a proposal that 'in the



light of these findings, there is not a very strong case for the continued use of etomidate either for anaesthesia or for longterm sedation'.[3] It is our opinion that this drug is useful in clinical anaesthesia as a continuous infusion in the absence of adverse effects[4] and the presence of cardiovascular stability and, in particular,[5] in those cases when we might take advantage of the *inhibition* of cortisol synthesis.[6-8]

Recently, in a patient with Cushing's syndrome, due to unilateral adrenonodular hyperplasia, on whom a left adrenalectomy was performed, we used a balanced anaesthesia induction with intravenous fentanyl (0.1 mg) and etomidate (0.3 mg/kg). Tracheal intubation was facilitated with suxamethonium (1 mg/kg), and for maintenance of anaesthesia a combination of air, oxygen, alcuronium and fentanyl was used, supplemented by an 0.02 mg/kg/minute infusion of etomidate. The adrenocortical function was studied during anaesthesia and in the recovery period and haemodynamic changes were monitored. There was a moderate peroperative decrease in serum cortisol levels, which returned to normal 8 hours later (Fig. 1) and, above all, the cardiovascular system was stable during surgery.

These data suggest that etomidate deserves further study, as an anaesthetic for patients with excess cortisol.

Department of Anaesthesia and Department of Endocrinology,
Hospital de S. Joao,
Porto, Portugal

J. Costa
D. Ramos
S. Massada
D. Carvalho
D. Pignatelli

References

1. Criado A, Maseda J, Navarro E, Escarpa A, Avello F. Induction of anaesthesia with etomidate: haemodynamic study of 36 patients. *British Journal of Anaesthesia* 1980; **52:** 803–6.
2. Ledingham I McA, Finley WEI, Watt I, Mckee JI. Etomidate and adrenocortical function. *Lancet* 1983; **1:** 1434.
3. Editorial. Etomidate. *Lancet* 1983; **2:** 24–5.
4. Moore RA, Allen MC, Wood PJ, Rees LH, Sear JW. Perioperative endocrine effects of etomidate. *Anaesthesia* 1985; **40:** 124–30.
5. Owen H, Spence AA. Etomidate. *British Journal of Anaesthesia* 1984; **56:** 555–7.
6. Wagner RL, White PF, Kan PB, Rosenthal MH, Feldman D. Inhibition of adrenal steroidogenesis by the anesthetic etomidate. *New England Journal of Medicine* 1984; **310:** 1415–21.
7. Wagner RL, White PF. Etomidate inhibits adrenocortical function in surgical patients. *Anesthesiology* 1984; **61:** 647–51.
8. Duthie DJR, Fraser R, Nimmo WS. Effect of induction of anaesthesia with etomidate on corticosteroid synthesis in man. *British Journal of Anaesthesia* 1985; **57:** 156–9.

Loss of consciousness after caudal injection

May I add to the discussion on the cause of loss of consciousness after caudal injection described by Dr Semple and Dr Bisset (*Anaesthesia* 1985; **40:** 380)? Speed of injection and large volumes of injectate were incriminated. Recent observations suggest that slow rates, and small volumes of injection may still cause large rises in intracranial pressure (ICP).

The effects of pressure transmission along the cerebrospinal axis were assessed in cadavers. Three 16-gauge epidural needles were inserted with the cadaver in the left lateral position. An injection needle was inserted to the L_{2-3} epidural space. A spinal sensing needle was inserted into the adjacent rostral space (L_{1-2}) with Huber point facing cephalad; this was used to measure spinal epidural pressure. The third needle was inserted into the cisterna magna using the technique described by Abrahams and Webb,[1] since cisternal pressure provides an accurate measure of ICP in the cadaver.[2] The cisternal and spinal sensing needles were each connected via three-way taps and 30-cm manometer tubing to separate Bell and Howells pressure transducers. The transducers were each taped in position to the midline of the cadaver and the zero control adjusted; they were then connected to parallel channels of a Devices twin-channel chart recorder.

Injections of 10 ml of 0.9% sodium chloride solution were made through the injection needle while the spinal

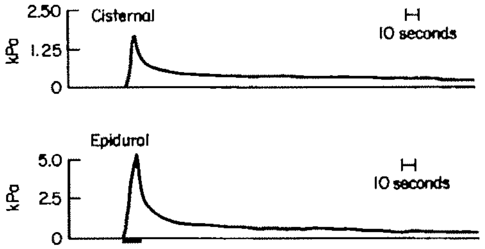


Fig. 1. Pressure recordings following epidural injection over 12 seconds with initial ICP of 0 kPa.

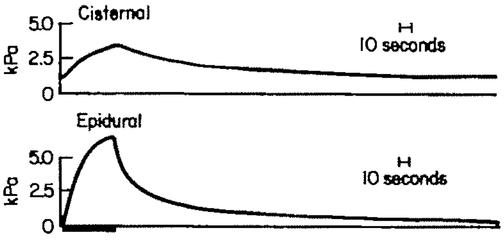


Fig. 2. Pressure recordings following epidural injection over 40 seconds with initial ICP of 1.0 kPa.

epidural and cisternal pressures were recorded. Injection was performed at zero ICP (Fig. 1). This showed a rapid rise and fall in ICP with epidural pressure. Injections were repeated after raising the ICP to 1.0 kPa using 0.9% sodium chloride. Subsequent injection showed an equally rapid rise in ICP with epidural pressure, but with a more prolonged plateau in ICP before return to a new, slightly raised level (Fig. 2). It should be noted that the rate of injection was slowed in order to obtain similar peak epidural pressure.

These observations extend those of Burn and Langdon (*Anaesthesia* 1985; **40**: 824) who measured spinal pressures two segments cephalad to large volume injectate. Large rises in ICP may, however, follow small volumes of injectate administered slowly; the important feature is the cerebrospinal compliance. Dr Zuck (*Anaesthesia* 1985; **40**: 923) describes the effects of acutely raised ICP after injection. Perhaps this phenomenon occurs in patients with underlying raised ICP or even with intracerebral pathology. It would be interesting to know whether any of these patients have undergone investigation for such lesions.

Department of Anaesthetics,
Royal Infirmary,
Edinburgh, EH3 9YW

P.A.J. HARDY

References

1. ABRAHAMS PH, WEBB PJ. *Clinical anatomy of practical procedures.* London: Pitman 1975.
2. MASSERMAN JH, SCHALLER WF. Intracranial hydrodynamics; experiments on human cadavers. *Archives of Neurology and Psychiatry* 1933; **29**: 1222–31.

Are armoured tracheal tubes really necessary for neuroanaesthesia?

It is customary in many anaesthetic departments to use armoured tracheal tubes for neurosurgical patients, and this practice is supported by standard texts on the subject. However, there does not appear to be any justification for this precaution when the patient's head remains stationary and the operative field does not encroach upon the airway. It should be possible, in my opinion, to maintain a clear airway using ordinary tracheal tubes.

To test this hypothesis, disposable implant tested tracheal tubes were used for a wide variety of neurosurgical patients who required anaesthesia and the patency of the airway was closely monitored. In adults, size 8.0, 8.5 or 9.0 mm internal diameter Mallinckrodt 'Lo Pro' tubes with low-pressure cuffs were used and in children plain tubes of the appropriate size were inserted, with oral packing if necessary. They were taped in place with plastic adhesive strapping and care was taken when positioning the head in order to avoid compression of the face or extreme flexion or extension of the neck. Bilateral air entry was checked and airway pressures were monitored continuously. Over one thousand cases have been recorded to date in a wide variety of postures common in neurosurgery.

One hundred and seventy-three major craniotomies were performed, 33 anterior cervical fusions and 73 posterior spinal decompressions anaesthetised in the prone position. In the radiology department, disposable tubes were used for angiography (femoral catheters) and CT scanning. Three pneumoencephalograms were carried out in the sitting position. Minor procedures included ventriculoperitoneal shunt insertion or removal, burr hole procedures and various wound explorations. The only malfunction recorded was one episode of cuff failure which was detected prior to use and a replacement was substituted with no further problems.

The conclusion drawn from these observations is that neurosurgical cases may be successfully managed without the use of armoured tracheal tubes. In addition, 20 patients who required postoperative respiratory support were spared unnecessary re-intubation at the end of the operation, and a larger number of patients may have benefited from the use of low-pressure tracheal cuffs during the longer operations. Moreover, it has been noted during the study that the plastic tubes far from tending to kink, become quite malleable at body temperature and conform to the patient's own airway. These results suggest that a larger trial is warranted which should include a cost-benefit comparison between the different types of tracheal tubes available to us. In the meantime, I would welcome the response of my colleagues in other neurosurgical centres to this challenge of a well-established custom which may be in need of review.

Department of Neuroanaesthesia,
Royal Hallamshire Hospital,
Sheffield S10 2JF

P.J. WRIGHT

Use of atracurium and labetalol in a patient with phaeochromocytoma

Atracurium would appear, on theoretical grounds, to be the suitable non-depolarising muscle relaxant for use during anaesthesia in patients with phaeochromocytoma. The arterial blood pressure may fluctuate during induction, intubation, positioning of the patient on the operating table and during surgical manipulation of the tumour. Hypertensive episodes may be accentuated by pancuronium and gallamine which cause tachycardia, and are therefore potentially hazardous. Atracurium does not have any effect on the heart rate[1] and would therefore seem to be the better muscle relaxant to use in cases of phaeochromocytoma.

A 37-year-old female presented with classical history of headaches, vomiting, pallor, palpitations and anxiety. Clinically, she was hypertensive with supine arterial blood pressure of 140/100 mmHg. Her 24-hour recording of ECG showed mainly ventricular ectopics with occasional supraventricular ectopics and occasional dropped beat. She was investigated for phaeochromocytoma and analysis of 24-hour urine collection showed levels of catecholamines diagnostic of phaeochromocytoma (urine normetanephrine of 141 μmol/24 hours; normal <5.5 μmol/24 hours). Intravenous pyelogram showed compression of upper pole of left kidney and CT of abdomen confirmed a 9-cm mass of tissue above the left kidney. She was immediately (three weeks before operation) started on phenoxybenzamine 20 mg twice a day and this was increased to 40 mg bd (two weeks before operation) to achieve a blood pressure of 140/90 mmHg and a pulse of 85/minute.

On the day of surgery the patient was premedicated with papaveretum 15 mg and hyoscine 0.3 mg intramuscularly one hour pre-operatively. Arterial and peripheral lines were established under local anaesthesia. Labetalol 40 mg was given intravenously before induction of anaesthesia. Anaesthesia was induced with thiopentone 200 mg followed by atracurium 50 mg. The patient's trachea was intubated and lungs ventilated with nitrous oxide and oxygen in 2:1 mixture with addition of 0.5% isoflurane. Increments of 10 mg of atracurium were repeated every hour. After induction of anaesthesia, an oximetric opticath catheter was inserted and pulmonary artery wedge pressure, central venous pressure (CVP) and venous oxygen saturation noted (20 mmHg, 12 cm H_2O and 70% respectively).

During the operation the pulse remained stable between 70 and 80 beats/minute. The diastolic blood pressure showed very little change and was in the range of 70–80 mmHg. During the entire two and a half hour procedure, the systolic pressure exceeded 150 mmHg only on three occasions, which were associated with surgical manipulation. On these three occasions labetalol 20 mg was given intravenously to keep the systolic pressure below 150 mmHg. The pulmonary artery wedge pressure rose to 26 mmHg on two occasions, both associated with a rise in systolic pressure. There was a decrease in mixed venous saturation to 54%, indicating a decrease in cardiac output during these hypertensive episodes. The CVP remained at 10–12 cm H_2O throughout. Paralysis was reversed and the patient's trachea extubated at the end of the procedure. There was neither hypertension nor tachycardia on extubation or in the immediate postoperative period. She was transferred to the intensive care unit where she remained stable and normotensive.

Atracurium provided satisfactory conditions during the procedure and labetalol was a useful drug in controlling the hypertensive episodes.[2] Pulmonary artery wedge pressure monitoring is not routinely used in perioperative management of patients with phaeochromocytoma. The preference is for the less aggressive method of CVP. This patient demonstrated the inability of CVP to reflect accurately the left-sided pressures and the usefulness of monitoring pulmonary artery pressures in patients with phaeochromocytoma.[3]

Department of Anaesthetics,
Royal Infirmary,
Aberdeen.

A. SHEIKH

References

1. HUGHES R, CHAPPLE DJ. The pharmacology of atracurium: a new competitive neuromuscular blocking agent. *British Journal of Anaesthesia* 1981; **53**: 31–44.
2. KAUFMAN L. Use of labetol during hypotensive anaesthesia and in the management of phaeochromocytoma. *British Journal of Clinical Pharmacology* 1979; **8** (Supplement 2): 229S–32S.
3. MIHM FG. Pulmonary artery pressure monitoring in patients with pheochromocytoma. *Anesthesia and Analgesia* 1983; **62**: 1129–33.

Pain on injection with droperidol and prevention of pain with etomidate

The letter from Dr Gauntlett (*Anaesthesia* 1985; **40**: 920–1) was interesting but it did not surprise me since I have been interested in this subject and since, after 3 years of trial and error, I have discovered a reliable technique for the avoidance of pain on injection with etomidate. However, during the course of my observations, pain on injection is occasionally caused by pretreatment with a combination of fentanyl 50 μg and droperidol 0.5 or 0.625 mg when they are given through the 23-gauge winged needle in the dorsum of the hand. Pain also occurs on injection with thiopentone, suxamethonium, and alcuronium, when given in this manner, but also on occasions when administered through a 16-gauge Venflon in the forearm. The mechanism is, I consider, similar. Rapid injection into a small vein, possibly constricted, is the cause, irrespective of the intrinsic properties of the drug. This is partly substantiated by the observations of Collins *et al.* on methohexitone.[2]

Pain on injection with etomidate is a common problem and occurs in about 30% of cases in whom no pretreatment or modification has been undertaken.

There is a regimen which virtually removes this problem and, at the same time, makes it suitable for day cases in whom premedication may be omitted. Once an intravenous route has been established, usually in the dorsum of the hand, a mixture of alfentanil 0.5 mg and droperidol 0.5 mg, is injected slowly. One should then wait until the mixture has had a chance to work, usually about 30 seconds, but it can be 2–3 minutes. The patient often notices a swimming sensation or even believes that anaesthesia is starting. It is important to wait until this effect has been observed otherwise failure of the pretreatment may occur.

A mixture of etomidate 20 mg with lignocaine 40 mg diluted with normal saline to make a 20-ml mixture is then injected slowly. The patient is asked if they are comfortable and examined for signs of discomfort, such as facial grimace, hand withdrawal or actual complaint of pain or burning. In 140 administrations this pretreatment has resulted in 3 complaints of mild discomfort or slight burning and, in each case, I did not wait for the obvious effects of the alfentanil and droperidol mixture.

This method is reasonably easy to undertake and especially effective. The use of the narcotic and droperidol mixture on its own caused, in a previous series of 170 administrations, a 12% incidence of pain. A similar figure of 12%, in 92 administrations, was obtained when 40 mg lignocaine and a 15-second tourniquet around the arm before the injection of etomidate were used, in contrast to the success reported reported by Burnell.[2] Alfentanil is particularly useful in unpremedicated cases and its action appears to be potentiated by the small dose of droperidol which also has an anti-emetic effect. Hiccups and involuntary muscular movement are not a problem.[3] Occasionally apnoea, which requires manual ventilation of the lungs, occurs but is usually brief.

Department of Anaesthesia, J.C. COGHILL
Plymouth General Hospital,
Plymouth, PL4 8QQ

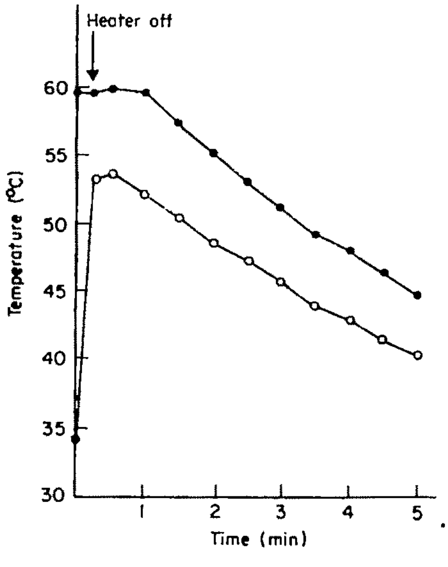
References

1. COLLINS KM, WILLATTS AG, GOULDING CA. Pain after injection. *Anaesthesia* 1983; **38**: 1002.
2. BURNELL JC. Pain after injection from methohexitone. *Anaesthesia* 1984; **39**: 286.
3. ANTONIOS WRA, INGLIS MD, LEES NW. Alfentanil in minor gynaecological surgery: use with etomidate and a comparison with halothane. *Anaesthesia* 1984; **39**: 812–5.

Another hazard of heated water humidifiers

The use of two very good items of equipment together, namely the Siemens Servo-900C and the Bennett Cascade 2 Humidifier, for heated vapour humidification in ventilated patients was not questioned until we recently observed that the humidifier alarmed during patient system disconnexions to allow tracheal suction. This was only during use of the ventilator in pressure controlled modes such as continuous positive airways pressure (CPAP), and did not occur during volume controlled ventilation. The patient inspired gas temperature alarm showed overheating and indeed the flow of gas felt hot. The combination of these two items of equipment used in this way was therefore considered to be unsafe and a heat and moisture exchanger was substituted for the heated vapour supplier, whereupon no further problems occurred.

In view of the potential thermal injury hazard to the patient's airway, a test rig was set up which consisted of a Siemens Servo-900C ventilator and a Bennett Cascade-2 Humidifier, running together at a room temperature of 22°C for one and a half hours, with settings of 10 breaths/minute, 3 litres/minute volume, a working pressure of 6.0 kPa, inspiratory time and inspiratory pause times of 25 and 10% of the respiratory cycle, 2.0 kPa trigger sensitivity below PEEP, and a PEEP of + 0.5 kPa. Separate thermocouples measured the temperatures of the water bath of the humidifier and of the patient end of the inspiratory system 45 cm proximal to the test lung. The length of the adult disposable plastic patient tubing was 110 cm from the humidifier to the temperature probe. Flow of gas through the system on disconnexion from the test lung was measured with a simple respirometer. The disconnexion flow was 53 litres/minute and was independent of whether the ventilator working pressure was 5,



6, or 7 kPa. On disconnexion and within 10 seconds, the humidifier patient temperature alarm sounded and switched the heater off. The temperature of the water bath before disconnexion was 59.4°C, and at the patient end of the system 34.2°C (as set). The rise in the patient system temperature and the time taken to fall to 40°C is illustrated in the Figure. Even though the water bath heater switched itself off in under 10 seconds it took 5 minutes for the patient system temperature to fall to 40°C.

Neither item of equipment was found to be malfunctioning. The large flow of gas in this ventilation mode on disconnexion has the unfortunate effect of carrying away an appreciable amount of thermal energy from the heat reservoir of the water bath. This problem could be avoided by occluding the patient end of the system during disconnexion or switching to a volume-controlled mode, but we felt that the potential for upper airway thermal damage (especially with children) on reconnexion made this system of humidification undesirable. We now only use heat and moisture exchangers (HMEs) with the Siemens ventilator.

The effectiveness of HMEs in mimicking the normal humidification processes of the upper airways, and the potential advantage of having a combined bacteriological filter within them is well known.$^{1-4}$ In our experience there has been no difficulty in obtaining tracheal aspirate nor evidence of tenacious secretions due to the use of HMEs in adults. In small children, regular tracheal instillation of 0.5 ml of physiological saline every 0.5–1 hour in addition has been found to be beneficial.[5] Therefore, because of the potential thermal injury hazard with heated vapour suppliers outlined above we have now relegated their use to that with simple minute volume divider ventilators. We recognise that some ventilators which produce much lower flow rates of fresh gas on disconnexion are in common use in paediatric areas and thus allow large losses of heat to occur in the patient system with little rise in temperature at the patient system with little rise in temperature at the patient end. What are others' experiences of this? Are we over-reacting? Why are such heated vapour suppliers still in such common use, especially in paediatric and special care baby units? With the advent of smaller neonatal sized HMEs, will this last bastion fall?

Hinchingbrooke Hospital,
Huntingdon,
Cambridgeshire, PE 18 8NT

H.S. Smith
R. Allen

References

1. Mapleson WW, Morgan JG, Hillard EK. Assessment of condenser-humidifiers with special reference to the multiple-gauze model. *British Medical Journal* 1963; **1:** 300–5.
2. Bethune DW. Hydrophobic versus hygroscopic heat and moisture exchangers. *Anaesthesia* 1985; **40:** 210–1.
3. Gilston A. Hygroscopic condenser humidifiers: value for money? *Anaesthesia* 1984; **39:** 1030–1.
4. Chalon J, Markham JP, Ali MM, Ramanathan S, Turndorf H. The Pall Ultipor breathing circuit filter—an efficient heat and moisture exchanger. *Anesthesia and Analgesia* 1984; **63:** 566–70.
5. Hatch DJ, Sumner E. *Current topics in anaesthesia. 5: Neonatal anaesthesia.* Edward Arnold, 1981.

Induction agent sensitivity and ophthalmoplegia plus

A 19-year-old patient who weighed 76 kg and was 1.72 m tall recently presented for surgery to correct his squint. He had a 4-year history of progressive external ophthalmoplegia (PEO) with marked bilateral ptosis and marked right divergent squint. There was some peripheral pigmentation of his retinae, a pulse rate of 45/minute (he did not take athletic training) and an unusual, non-specific intraventricular conduction pattern on the ECG. It was considered that he was suffering from ophthalmoplegia plus, probably of a Kearns-Sayre type (PEO, retinitis pigmentosa and heartblock).[1]

Premedication was with 2 mg levorphanol and 0.4 mg hyoscine intramuscularly. He was brought to theatre and given intravenous atropine 0.6 mg. In view of my previous experience of sensitivity to thiopentone in a case of ophthalmoplegia plus,[2] anaesthesia was induced with etomidate intravenously. The lash reflex was lost after 4 mg had been given slowly. Intravenous suxamethonium 100 mg was used to facilitate tracheal intubation. The patient then breathed spontaneously from a circle absorber system with 2% halothane. The operation was uneventful.

The recommended induction dose of etomidate is 0.3 mg/kg; this would have given a total dose of 23 mg which is more than five times that which was required. Premedication had been with normal doses in relation to the patient's weight. This patient was not taking any medication unlike the previous reported patient.

Undue sensitivity to two different anaesthetic induction agents suggests that, in this condition, all induction agents should be used slowly, in small dosage.

Leicester Royal Infirmary,
Leicester LE1 5WW

R.H. James

References

1. Rose FC. *The eye in general medicine.* London: Chapman and Hall, 1983; 162–5.
2. James RH. Thiopentone and ophthalmoplegia plus. *Anaesthesia* 1985; **40:** 88.

A modification of the linear analogue

The linear analogue is recognised as an acceptable method of rating pain or anxiety and its reliability for evaluating pain was established by Revill *et al.*[1] The technique involves the use of a straight line 10 cm in length. One end of the line represents absence of pain (anxiety) and the other end the maximum pain (anxiety) the patient can imagine. The patient expresses the pain (anxiety) he has by making a perpendicular mark on the line.

We used the linear analogue to study the effect of oral lorazepam on pre-operative anxiety. Our patients, who were mostly women from rural areas, had little or no formal education and found it very difficult to express their anxiety by means of the linear analogue used in the conventional manner. They were, however, able to express their anxiety by drawing a line from the zero mark parallel to the printed 10-cm line. The length of the line they drew represented the extent of their anxiety and provided a scale value for comparison.

It would seem that for a semiliterate population, this modification of the conventional linear analogue offers more reality.

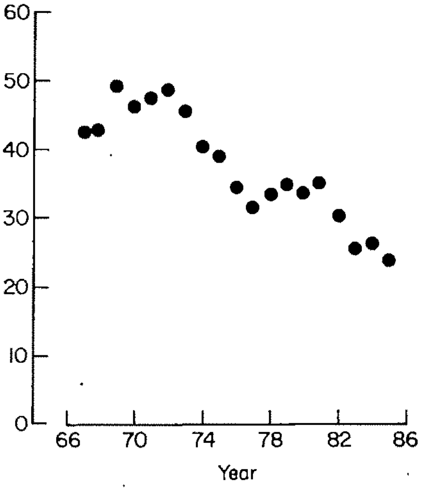
General Hospital,
Kalutara,
Sri Lanka
J.P. JAYASURIYA

Reference

1. REVILL SI, ROBINSON JO, ROSEN M, HOGG MIJ. The reliability of a linear analogue for evaluating pain. *Anaesthesia* 1976; **31:** 1191–8.

Pass rates in the final FFARCS examination

Dr Grant (*Anaesthesia*, 1985; **40:** 823–4) draws attention to the decrease seen since 1977 in the pass rate for the final FFARCS examination. The accompanying figure shows that this is not a recent phenomenon. Early in the 1970s, pass rates approached 50%; in 1985 the overall rate was less than 25%.



It is perhaps more useful to look at the overall numbers of new fellows. From 1971 to 1975 there were 927 passes; from 1976 to 1980 these were 1018 and from 1981 to 1985, 1104. An expansion still, despite the falling pass rate.

Dr Grant suggests four reasons why the rate is declining. First, he suggests that the standards of candidates is falling. This is difficult to prove or disprove; my impression is that the standards of new entrants into anaesthesia is improving. His second reason is that training throughout the country is failing to keep up with the increased knowledge required for the examination. This is possible. Certainly most departments are experiencing an increase in the service work and in the complexity of that work. This could reduce teaching. One measure can, however, lead to a rapid improvement in the training needed to pass any examination. The local tutors should attend the examinations, as is their right, since the view from the side of the green baize differs from that of the candidates and of the examiners.

Thirdly, he suggests that the standard for the examination is being raised deliberately, in order to regulate the number of candidates applying for senior registrar posts. This I can refute. As an examiner for the last 7 years, I have never had any instruction about the number of successful candidates and I doubt if any examiner has, or if any could accept, such an instruction. Standards are rising certainly; knowledge of anaesthetic physiology, pathology and pharmacology grows each year and candidates and their teachers should keep abreast of what is going on.

Dr Grant's last point is a question as to whether the final FFARCS should be the mechanism regulating entry into the higher grades. It seems ineffective at the moment, when each post attracts up to forty or more applicants. However, we are not yet approaching the problem seen in general surgery,[1] in which discipline it was found that of 66 applicants for a senior registrar post, 57 had undertaken full time research and 24 had a degree or diploma such as an MS as well as the fellowship.

It is my belief that the FFARCS should be regarded as a guarantee to the public that its holder has the knowledge to deliver a high standard of anaesthetic care and has the ability to improve that standard over the rest of his career. It is an international standard and should not be looked on only in terms of staffing hospitals in the United Kingdom.

Whether it should have two or three parts is a matter that time will decide.

Shackleton Department
of Anaesthetics,
The General Hospital,
Southampton SO9 4XY

J. NORMAN

Reference

1. TAYLOR I, CLYNE CAC. Applications for senior registrar posts. *British Medical Journal* 1985; 2: 143–4.

A computer-generated guide for paediatric anaesthesia

For many years we have been calculating fresh gas flow rates, drug doses and the parameters required for fluid management before induction of anaesthesia in our paediatric patients. This has been recommended by others[1] and is sound practice since it provides guidelines and avoids potentially disastrous miscalculations, which may be made under stress in the operating room, especially by persons unfamiliar with the necessary formulae. Three years ago the process was computerised to produce a worksheet for everyday use. It has, in the light of experience, been updated and modified to produce a simple clear print out which has been widely and enthusiastically received by our consultants, registrars and nurse anaesthetists.

We noted with interest the publication by Kraemer and Stead,[2] but consider their resulting print out too detailed and possibly confusing for routine use, especially for those who do not manage paediatric cases on a daily basis. Because of the special requirements of the neonate, the operator may select a worksheet for patients under 30 days of age, or one for infants and children up to 30 kg body weight. This provides guidance about tracheal tube sizes, fresh gas flow rate, initial and incremental dosages of drugs, fluid and blood replacement, anticipated urinary losses, and resuscitative regimens. The required variables are the patient's name, age, weight, hours with oral intake and haematocrit. We use an Apple II c computer with 128K RAM, a single disk drive and a printer placed in a convenient location within the operating suite. The program is available on diskette in Applesoft Basic and in advanced Basic on diskette (MS DOS 2.0 or higher) for use with an IBM PC or compatible computer. It is also available on a tape cassette in Radio Shack Basic for use with their TRS80 Model PC2 pocket computer with printer. (10K RAM) Enquiries should be addressed to the author.

Department of Anesthesiology,
Duke University Medical Center,
Durham, North Carolina 27710 U.S.A.

E.C. BLOCH

References

1. SMITH RM. *Anesthesia for infants and children*. 4th edn. St. Louis: C.V. Mosby, 1980; 547–83, 666–71.
2. KRAEMER CA, STEAD SW. Computer-assisted pediatric worksheets for anesthesia. *Anesthesiology* 1984; 60: 520–2.

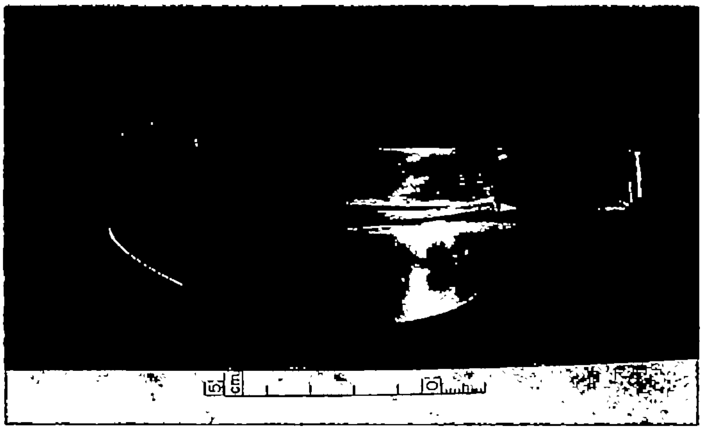
Modification of laryngoscope for nasogastric intubation

Dr Campbell and Dr Millar's description (*Anaesthesia* 1985; 40: 703–4) of a laryngoscope blade modified to aid nasogastric tube insertion in the intubated patient was interesting since I also had reflected on the need for such an instrument, but hit upon a different solution.

This manoeuvre (insertion of a nasogastric tube in an intubated patient) is a stimulating procedure, often associated with a marked pressor response in the patient, which is potentially detrimental in the high risk patient. The problem is not only to obtain a direct view of the oesophageal opening, but also to have enough room to manipulate using Magill's forceps to advance the nasogastric tube past that part of the oesophagus partially compressed by the inflated tracheal cuff. Good conditions enable the manoeuvre to be performed as quickly and deftly as possible.

With the Campbell and Millar modification, although the view may be good, space for manipulation with Magill forceps is limited because the tracheal tube sits on the right side of the oropharynx. If the tongue and tracheal tube are pushed to the left side of the oropharynx, the conventional Macintosh blade flange is too narrow to hold them both, and the view is often blocked when the tongue falls off the blade. My solution to the dilemma is to widen the Macintosh blade flange.

The blade is tapered, and is one centimetre wider than usual where the bulk of the tongue sits, and is narrow where a good view is required, at the oesophageal end. The flange width at the dental end is unchanged. There is no greater risk of oral trauma. The wider flange keeps both tongue and tracheal tube out of the way, and gives a good view and plenty of space for manipulation with forceps. Several colleagues have used this blade and



commented favourably on its ease and convenience.

The new shape blade was made up in the Engineering Department, and it was not necessary to move or alter the light source.

Department of Anaesthesia,
Royal Perth Hospital,
Perth,
Western Australia 6001

FIONA MCWHINNIE

A mistaken case of hypersensitivity to a local anaesthetic

A 20-year-old full term, gravida two lady, with a history of atopic asthma was admitted in spontaneous labour. She had had an epidural analgesia with bupivacaine 3 years previously, without any problems. Her drug therapy included salbutamol inhalation as required. She had been in hospital, in the past, for status asthmaticus and had required steroids but not intermittent positive pressure ventilation of her lungs. There was no evidence of bronchospasm.

Syntocinon infusion was started to augment labour and epidural catheterisation was performed 150 minutes later for pain relief. A test dose of 4 ml bupivacaine 0.5% plain was followed by another 4 ml. Good pain relief was achieved. A further top-up of the same drug was administered 90 minutes later. Forty minutes following the second top-up marked urticaria appeared on her forearms and rapidly became generalised. She developed marked bronchospasm and complained of a constricting feeling in the neck which suggested laryngeal oedema. Syntocinon was discontinued and no further bupivacaine was given, in case either of these drugs were responsible for the patient's allergic response. Hydrocortisone 300 mg and chlorpheniramine 10 mg were administered intravenously. The bronchospasm was relieved completely by inhalation of two metered doses of salbutamol (200 mg). Hypotension did not occur, although transient fetal bradycardia was recorded. The urticaria improved over the next 60 minutes. Analgesia was provided by Entonox and she had an uneventful delivery and puerperium.

Later, it was revealed that a change of midwife occurred just before the patient developed bronchospasm and urticaria. This midwife admitted to having a pet dog at home. The patient reported an episode following contact with dog hair 2 years previously, for which she was admitted to hospital. She had also received local anaesthetic injections in the past for dental surgery but did not have any reaction. Differential count on the next day showed 2% eosinophils.

Four weeks later, intradermal and patch tests were performed on the patient. The patient showed a marked sensitivity to dog, cat and horse hair, pollen and feathers. She did not show any skin reaction to bupivacaine (Marcain), lignocaine or syntocinon. Serum IgE, IgA, IgE and IgM levels were within normal limits. The patient was told that she was not allergic to bupivacaine and lignocaine and reassured that she could have epidural analgesia during a future labour.

True allergy to local anaesthetics is rare, but there are many recorded cases of hypersensitivity to them.[1-3] We could find only one established case of bupivacaine hypersensitivity.[4] Allergy to syntocinon is extremely rare but there is one reported case.[5]

There are two lessons to be learnt from this case. Firstly, if proper circumstantial evidence (the allergy to dog's hair and the presence of the midwife with a pet dog at home) was enquired for, the patient could have had the benefit of epidural analgesia throughout the labour. In this case, it was abandoned once the reaction occurred. Secondly, if the patient had not been tested by intradermal testing, she would have been falsely labelled 'allergic to bupivacaine'.

Department of Anaesthetics,
University Hospital,
Nottingham NG7 2UH

Y. MEHTA
M.C. LUXTON

References

1. Noble DS, Pierce GFM. Allergy to lignocaine. A case-history. *Lancet* 1961; **2:** 1436.
2. Aldrete JA, Johnson DA. Allergy to local anesthetics. *Journal of the American Medical Association* 1969; **207:** 356–7.
3. Walker RT. Hypersensitivity reaction to local anaesthetic. *British Dental Journal* 1971; **130:** 2.
4. Brown DT, Beamish D, Wildsmith JAW. Allergic reaction to an amide local anaesthetic. *British Journal of Anaesthesia* 1981; **53:** 435–7.
5. Slater RM, Bowles BJM, Pumphrey RSH. Anaphylactoid reaction to oxytocin in pregnancy. *Anaesthesia* 1985; **40:** 655–6.

Ulnar nerve stimulation in the thick arm

Dr Hunter and her colleagues (*Anaesthesia* 1985; **40:** 916) raise an interesting point about stimulation of the ulnar nerve in the forearm of oedematous, and also in obese or muscular, patients. The use of needle electrodes might conceivably result in direct stimulation of the muscle or damage to the nerve. My practice in this circumstance is to connect the positive electrode of the neurostimulator to a paste electrode over the medial epicondyle, rather than to the orthodox position of the wrist region. The ulnar nerve passes in close proximity to the electrode at the elbow and the response of the muscles, if it is to be seen at all, is good.

Department of Anaesthesia, D.A. Cozanitis
Helsinki University Central Hospital,
SF-00290 Helsinki 29,
Finland

Failure of injection during attempted spinal anaesthesia

Difficulties may be experienced at several stages during attempted spinal anaesthesia. We would like to report a previously unrecorded problem encountered while performing a spinal anaesthetic.

A 36-year-old primigravida with a past history of an ectopic pregnancy presenting for lower segment Caesarean section requested epidural anaesthesia. Unfortunately, this proved unsuccessful after a total dose of 27 ml 0.5% bupivacaine (135 mg) had been given. The patient wanted to be awake for the birth of her child so it was decided to proceed with spinal anaesthesia. A 25-gauge, 6.3 cm disposable spinal needle was inserted at the L_{3-4} interspace. At approximately 6 cm a click was felt and the introducer was removed. Clear fluid slowly filled the hub of the needle but did not spontaneously drip any further. A 2-ml syringe containing 1.5 ml heavy cinchocaine (7.5 mg) was attached to the needle hub. Clear fluid was easily aspirated through the needle which mixed with local anaesthetic, so injection of the local anaesthetic was attempted but proved impossible despite firm pressure being applied to the syringe.

The needle was then rotated through 180°, and although aspiration through the needle was still possible, injection through the same needle was not. The patient had no paraesthesiae, so the introducer was reinserted and the needle advanced a further 1–2 mm. When the introducer was removed, clear fluid dripped slowly from the needle hub, but on attaching the syringe, injection of local anaesthetic again proved impossible. The needle was again rotated through 180°, but despite the aspiration of clear fluid, injection through the needle remained impossible. The spinal needle was then replaced and spinal anaesthesia via the new needle was achieved without any problems. This produced a sensory block to T_6 and the operation was successfully performed.

When the first needle was attached to another syringe it was again possible to aspirate air through the needle but attempted injection remained impossible. Examination of the bevel of the needle failed to reveal any abnormality, and examination of the needle lumen viewed through the needle hub showed it to be patent.

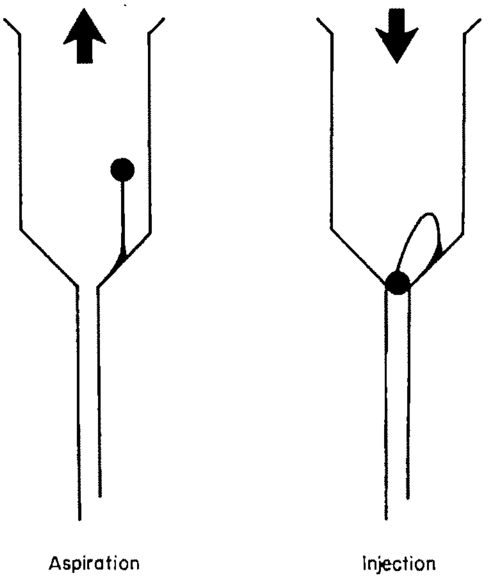


Fig. 1. Mechanism of 'ball valve' effect due to blood clot during attempted injection through a spinal needle.

Close examination of the inside of the needle hub revealed a small pedunculated blood clot adherent to the side of the needle (Fig. 1).

The problems with aspiration of, or injection into, the cerebrospinal fluid (CSF) during spinal anaesthesia, once the dura has been penetrated, are usually due to occlusion of the spinal needle by dura or by one of the nerve roots of the cauda equina.[1-3] This, however, usually presents as difficulty with aspiration of CSF rather than difficulty with injection of the local anaesthetic agent, and is usually overcome by twisting the needle through 180° and/or advancing it slightly.[2]

The repeated ease of aspiration but difficulty with injection suggested a ball valve effect, but any problem with the needle itself appeared unlikely because of the repeated passage of the introducer through the needle. The only explanation, however, is that a ball valve effect was due to the pedunculated blood clot present in the needle hub, which occluded the needle during injection but was free during aspiration. The blood clot appeared to be adherent to the inside wall of the needle hub as shown in Fig. 1, and so was not dislodged by the insertion of the introducer.

The only other cause of difficulty with injection after easy aspiration of CSF apparent from a review of the literature, involved a patient whose CSF had been contaminated with Pantopaque® (isomers of ethyliodophenylundecolate) used for a myelogram 18 years previously. It was thought that the radiological dye reacted with the rubber in the plunger of the syringe and made injection difficult after straightforward aspiration.[4]

In view of the increasing use of fine bore needles for spinal anaesthesia, the pattern of a ball valve effect from small blood clots should be considered as a cause of difficulty with injection into the CSF.

Shackleton Department of Anaesthetics,
Southampton General Hospital,
Southampton SO9 4XY

N.C.T. WILTON
T.S. BROWN

References

1. ADRIANI J. *Labats regional anesthesia: techniques and clinical applications*, 3rd edn. Philadelphia and London: W.B. Saunders; 1967.
2. LUND PC. *Principles and practice of spinal anesthesia.* Illinois: Charles C. Thomas, 1971.
3. MACINTOSH R, LEE JA. Lumbar puncture and spinal analgesia. 3rd edn. Edinburgh and London: Churchill Livingstone, 1973.
4. GLICK RV. An unusual cause for increased resistance to injection during administration of spinal anesthesia. *Anesthesiology*, 1982; **57**: 64–5.

Tracheal administration of drugs

The tracheal use of drugs in cardiopulmonary resuscitation was first studied in 1967[1] and is mentioned in both the 1974 and 1980 American Heart Association Standards for Cardiopulmonary Resuscitation and Emergency Cardiac Care. At present, the tracheal use of resuscitation drugs (atropine, adrenaline, lignocaine) is recommended in situations where it is not possible to establish any peripheral or, preferably, central venous access. Such situations arise primarily in management of patients outside hospital by paramedical personnel in North America, and also, for example, in small children or the obese. The tracheal route may be considered to be safer than intracardiac injection and the subject has recently been reviewed.[2]

The letter by Berlot *et al.*, about the use of naloxone in cardiorespiratory arrest (*Anaesthesia* 1985; **40**: 819) is of interest, but we fail to understand their choice of the tracheal route for the administration of the drug. The patient described in the case report was suffering from haemorrhage as a result of ruptured oesophageal varices. Peripheral venous access was present and naloxone, if indicated, could have been given by this route, or preferably by a central venous line which would be essential for the successful management of such a patient. Too little information is given about the second patient described to allow comment.

The technique of tracheal drug administration has been investigated.[3,4] Drugs should be diluted in not more than 10 ml of normal saline and delivered so as to be dispersed as distally as possible in the lung. Jones and Bray (*Anaesthesia* 1985; **40**: 921) suggest a Portex remote injection catheter, but we have found this is difficult to pass and it curls up within the tracheal tube. An epidural catheter is satisfactory but a small bore suction catheter is a cheap and ready alternative. These can be passed through a Portex 15 mm Fibreoptic Bronchoscope Swivel connector. In North America, a catheter spray device is commercially available. Following installation 5–10 forceful rapid ventilations are necessary to aid dispersion to both lungs[4] and rapid absorption.

Hammersmith Hospital,
Ducane Road,
London, W12 OH5

M.B. TAYLOR
D.A. ZIDEMAN

References

1. REDDING JS, ASUNCION JS, PEARSON JW. Effective routes of drug administration during cardiac arrest. *Anesthesia and Analgesia* 1967; **46**: 253–8.
2. GREENBERG MI. The use of endotracheal medical in cardiac emergencies. *Resuscitation* 1984; **12**: 155–65.
3. GREENBERG MI, BASKIN SI, KAPLAN AM, URRICHIO F. Effects of endotracheally administered distilled water and normal saline on the arterial blood gases of dogs. *Annals of Emergency Medicine* 1982; **11**: 600–4.
4. GREENBERG MI, SPIVEY WH. Comparison of deep and shallow endotracheal administration of dionosil in dogs and effect of manual hyperventilation. *Annals of Emergency Medicine* 1985; **14**: 209–12.

Topical lignocaine after tonsillectomy in children

Tonsillectomy in children is a painful, sometimes traumatic, procedure. We wondered if topical analgesia of the tonsillar bed would provide pain relief in the immediate postoperative period before systemic analgesics became effective. This would avoid the suppression of the cough reflex due to narcotics administered intra-operatively. There are reports of surgeons infiltrating the tonsillar bed with local anaesthetic,[1] but no reports have been found of the use of topical anaesthesia. Forty-nine children, listed for tonsillectomy and in most cases adenoidectomy, were divided into two groups on a random basis. The children all had a standard anaesthetic without premedication, induction with thiopentone and suxamethonium or halothane followed by tracheal intubation and maintenance with nitrous oxide, oxygen and isoflurane. No other drugs were administered intra-operatively. Laryngoscopy was performed after the operation, so that the pharynx and larynx could be cleared of blood and secretions. The patients in the first group had the tonsillar beds sprayed with 10% lignocaine spray to a total dose of 2 mg/kg. The patients in the second group were not sprayed and acted as the control group.

The children were taken to the recovery room after tracheal extubation and were assessed by one of the two investigators who were unaware to which group the patients belonged. Assessment continued over the first 15 minutes. Each patient was observed for restlessness, coughing and stridor. Each modality was judged as absent, mild, moderate or severe. A score of zero was given if the modality was absent and three if severe. The maximum score was therefore nine. The results were statistically analysed using the Chi square test.

Pain in children is difficult to assess, as in most cases it is impossible to achieve the co-operation required to use the linear analogue for evaluating pain.[2] A questionnaire for scoring pain was initially used but this proved impractical.[3] It was therefore decided to evaluate pain and discomfort on a global scale, using the degree of restlessness as a guide. Systemic absorption of the lignocaine might also have an effect in the reduction of stridor and laryngospasm after extubation since it is known that, when administered intravenously, lignocaine may have this effect.[4]

Codeine or pethidine was nearly always administered intramuscularly to the children in the recovery room. The peak effect after intramuscular injection is usually 15–30 minutes after administration, so this was unlikely to be effective over the period of assessment.

The results show that there was a significant difference between the two groups ($p < 0.02$) with regard to restlessness, but no significant difference between the groups with regard to stridor or coughing. It would therefore seem apparent that 10% lignocaine spray, when administered topically to the tonsillar bed following surgery, is effective in the reduction of general discomfort of the patient in the immediate postoperative period. It does this without impairing reflex protection of the airway.

Royal Gwent Hospital,
Newport,
Gwent, NPT 2UB

ALISON WILLIAMS
A. HAMILTON

References

1. DONLAN JV, JR. Anaesthesia for eye, ear, nose and throat surgery. In: Miller R.D., ed. *Anaesthesia.* Edinburgh: Churchill Livingstone, 1981: 1303.
2. REVILL SI, ROBINSON JO, ROSEN M, HOGG MIJ. The reliability of a linear analogue for evaluating pain. *Anaesthesia* 1976; **31:** 1191–8.
3. AUSTIN KL, STAPLETON JV, MATHER LE. Multiple intramuscular injections: a major source of variability in analgesic response to meperidine. *Pain* 1980; **8:** 47–62.
4. BARAKA A. Intravenous lidocaine controls extubation laryngospasm in children. *Anesthesia and Analgesia* 1978; **57:** 506–7.

Labelling of drugs

It was with interest that I read Dr Rendell-Baker's letter (*Anaesthesia* 1985; **40:** 912–3). When drugs are to be administered to a patient, it is the clinician's duty to check that he is giving what he thinks he is giving before he does so. User-applied labels on syringes maintain the identity of a drug, once drawn up and, for this purpose, plain labels with conspicuous lettering will suffice.

It might be more sensible if ampoules were of a simple uniform design, with large lettering to identify the contents. Complexity breeds mistakes and coloured labels necessitate colour vision. Simplicity may go some way to ensure labels are read and unfortunate accidents avoided.

Department of Anaesthetics,
University College Hospital,
London, WC1E 6AU

M.J.A.PARR

Hazard from the oxygen flush control

Signs of light anaesthesia and unwanted PEEP were observed during an intra-abdominal procedure on a child, when a coaxial Mapleson E system and mechanical ventilation of the lungs were in use. Rotameter,

Fig. 1

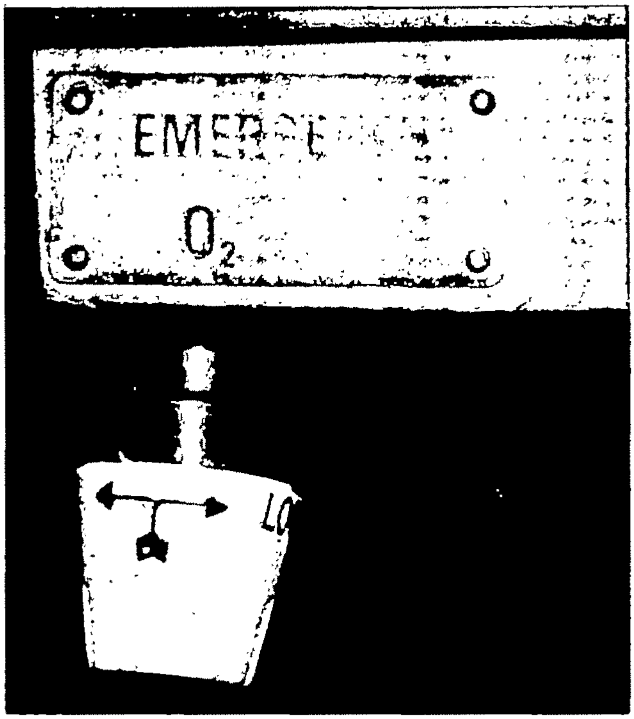
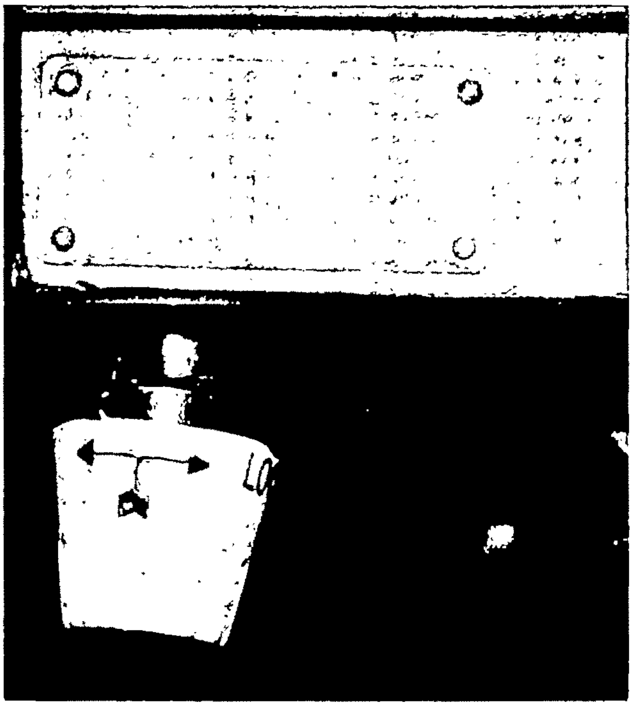


Fig. 2



vaporizer, and ventilator settings, breathing system connexions and end-tidal CO_2 readings were checked and no fault was detected. On disconnecting the fresh gas tubing from the swivel outlet of the Boyle's machine, however, an unexpectedly high gas flow was delivered. One immediately suspected the oxygen flush device which was found to be stuck in a partially open position, despite not having been turned axially to its locking position. The knob was pulled out to its normal 'off' position and the anaesthetic proceeded uneventfully.

On subsequent examination it was found that the spindle of the oxygen flush device had been bent (Fig. 1), presumably due to an impact sustained while moving the machine. As a result, moderate pressure on the knob caused it to remain in a partially open position (Fig. 2), owing to binding of the spindle. In the latter position, oxygen flow was measured at between 20 and 30 litres/minute, which accounted for the light anaesthesia and undesired PEEP. Detection of the fault condition would have been aided by use of an oxygen analyser in the breathing system.

The oxygen flush device of a Medishield Boyle's machine would seem to be particularly liable to this type of damage. The hazard could be eliminated by a redesign of the device, by transfer to a less vulnerable position. Furthermore, it would seem prudent to include a simple check of oxygen flush function as a conclusion to one's routine safety tests of Boyle's machines before use.

Department of Anaesthetics,
University Hospital of Wales,
Cardiff, CF4 4XW

N. Puttick

A tunnelling technique for central venous catheters

The technique and advantages of subcutaneous tunnelling have been demonstrated[1–4] and tunnelling of central venous catheters has thus become a common procedure. We routinely use Vygon Nutricath-S catheters inserted via the subclavian route for percutaneous central venous access and parenteral nutrition. If the introducer supplied with the catheter is used in the conventional way to form a subcutaneous tunnel, catheter puncture or transection may result, devices used for epidural catheters have been employed to overcome this problem.[5] We have modified our technique to avoid catheter trauma whilst using the introducer provided with the catheter.

Subclavian puncture is performed through a small skin incision and the catheter inserted in accordance with the manufacturer's instructions. A subcutaneous tunnel 8–10 cm long is formed by inserting the introducer needle through the skin incision and directing it

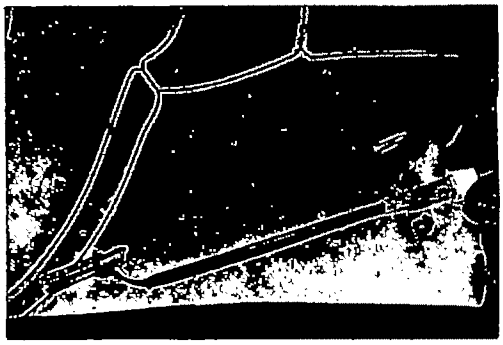


Fig. 1

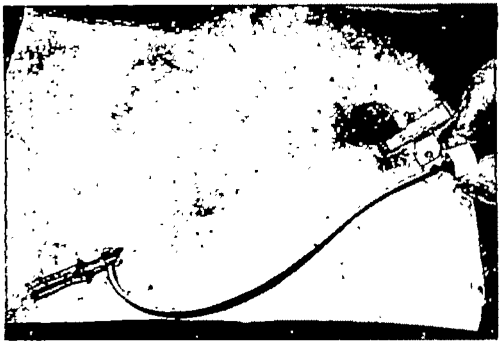


Fig. 2

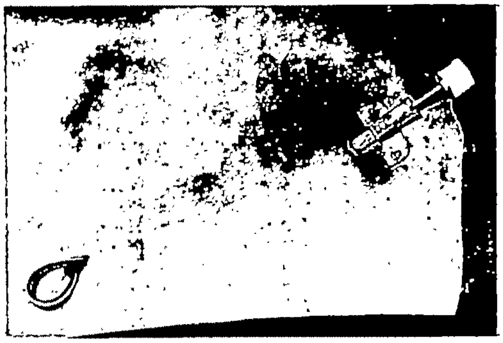


Fig. 3

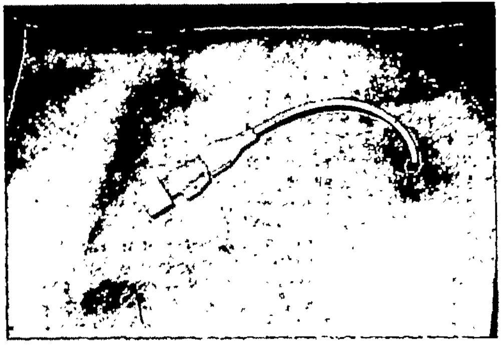


Fig. 4

away from the catheter towards the intended cutaneous exit site (Fig. 1). The introducer sheath is then inserted in a retrograde manner over the needle (Fig. 2). The needle is removed and the catheter is passed through the external sheath (Fig. 3). The Luer lock connector is attached to the catheter and the skin incision closed with a suture (Fig. 4).

This technique avoids catheter trauma and requires no additional equipment. We hope others will find it useful.

Department of Anaesthesia, N.M. Woodhall
The Royal Marsden Hospital, D.R. Redman
London, SW3 6JJ

References

1. Titone C, Lefton C, Sakwa S. A technique for chronic subclavian vein catheterization. *Surgery, Gynecology and Obstetrics* 1973; **137**: 489–90.
2. Powell-Tuck J. Skin tunnel for central venous catheter: non-operative technique. *British Medical Journal* 1978; **1**: 625.
3. McLean Ross AH, Anderson JR, Walls ADF. Central venous catheterisation. *Annals of the Royal College of Surgeons of England* 1980; **62**: 454–8.
4. Smith V, Smith MF, Lindop MJ. Central venous catheterisation using the subcutaneous tunnelling technique. *British Journal of Intravenous Therapy* 1983; **2**: 7–13.
5. Tonkin PA, Smith GB, Grimes AP. A subcutaneous tunnelling device for central venous catheters. *Anaesthesia* 1984; **39**: 196–7.

Diluting suxamethonium

There is a potential problem inherent in the common practice of dilution of suxamethonium before use, for example, in paediatrics or for a suxamethonium infusion.

During a recent all-day list, I prepared two dilute 'stock' solutions of suxamethonium (10 mg/ml), each prepared by adding 2 ml of suxamethonium (Anectine; 100 mg) stored in the refrigerator, to 8 ml saline stored at room temperature. The first patients after lunch, a child weighing 18 kg, needed tracheal intubation with suxamethonium and, since there was some of the morning stock solution left, it was inadvertently used. After a thiopentone induction, 30 mg suxamethonium was injected intravenously. There was no relaxation, and the child continued to breathe spontaneously. A further 30 mg suxamethonium was injected, again with no effect; the stock solution had worked perfectly well, as judged clinically, during the morning list. The child's trachea was therefore intubated during spontaneous ventilation of nitrous oxide, oxygen and halothane and a new stock solution (10 mg/ml) was made up using a 'fresh' ampoule from the same packet of suxamethonium used previously. A further 30 mg of suxamethonium was then injected intravenously through the same cannula, whereupon the child was promptly paralysed.

It was concluded that the suxamethonium used to make the morning's stock solution had been inactivated by standing for 5 hours at room temperature and that this process was hastened by dilution with saline stored at room temperature. It seems likely, therefore, that the tachyphylaxis occasionally encountered when using a suxamethonium infusion (1 mg/ml) is due, at least in part, to some degree of inactivation caused by warming, particularly if the suxamethonium is diluted with saline stored at room temperature, as is usually the case.

When suxamethonium is diluted to facilitate correct dosage in children, then ampoules of cold saline should be used. However, when suxamethonium is diluted for use as an infusion it is then, unfortunately, undesirable to use very cold saline in view of the volume to be used. A compromise is necessary and, in practice, saline stored in a cool place is generally quite adequate.

Department of Anaesthetics, R.W.D. Nickalls
Newcastle General Hospital,
Newcastle-upon-Tyne, NE4 6BE

Rough and ready

A recent experience in connexion with direct arterial blood pressure monitoring may be of interest to readers. No devices for continuous infusion of arterial cannulae were available (the last one had been used the day before) and so, rather than abandon the method, the following procedure was adopted. A knot was tied in the tubing from the reservoir of heparinised saline and this was connected to one limb of the three-way tap, the other two attached to the pressure transducer and to the cannula in the patient's radial artery. The infusion bag was pressurised to 300 mmHg, the knot pulled tight and the customary roller valve used to slow the flow rate to a rate which approximated to that normally allowed by the commercial device.

In the best of all possible worlds one never exhausts the supply of important pieces of equipment but in this case the patient with multiple injuries and direct thoracic injuries was saved from further damage from frequent arterial punctures and had the benefit of continuous monitoring.

Dunfermline and West Fife Hospital, K. Birkinshaw
Reid Street,
Dunfermline KY12 7EZ

Resuscitative skills

Dr Barcroft is to be congratulated on drawing attention to the deficiencies in resuscitative skills of young house officers and nurses and for his suggested remedy of supervising them in bag and mask ventilation of surgical patients prior to intubation in the anaesthetic room (*Anaesthesia*, 1985; **40**: 1015–6). May I suggest that the ideal list on which such teaching can be practised, of course under the expert guidance of the anaesthetist, is the E.C.T. list. In patients undergoing this form of treatment, the management of apnoea following the injection of the induction agent and the relaxant, before the application of the current, and then after the convulsion until adequate ventilation is fully restored, offers an excellent opportunity for this form of teaching bag and mask ventilation to young doctors and nurses. It also adds to the interest of what may otherwise be a rather routine session.

Department of Anaesthetics,
Southend Hospital,
Southend SS0 0RY

J.A. LEE

Anaesthesia, 1986, Volume 41, pages 227–228

Book reviews

A Calculus of Suffering 227
M.S. Pernick
Care of the Postoperative Surgical Patient 227
Edited by J.A.R. Smith and J. Watkins
Opioids in Anaesthesia 228
Edited by F.G. Estafanous
600 MCQs in Anaesthesia: Basic Sciences 228
P.J. Simpson and N.W. Goodman

A Calculus of Suffering

M.S. Pernick. Pp. 421. Columbia University Press, 1985. US$45.5

Following Morton's demonstration that the inhalation of ether vapour could prevent the pain of operative surgery, it is well known that news of the discovery spread rapidly and widely. Yet this event did not lead to an end of suffering during every operation of any magnitude for many years. This point has, of course, been made before. It is, nevertheless, chilling to the modern reader to learn that as late as 1873 amputations of the leg were undertaken without the use of an anaesthetic by a New York surgeon who had, over the previous 26 years, used anaesthesia, but only in selected cases.

Amongst the several great merits of Mr Pernick's scholarly work is the notable thoroughness with which he has explored the medical profession's attitudes to the use of anaesthesia and, indeed, the more general question of its attitudes to suffering during the nineteenth century in America. He analyses how these attitudes changed as industrialisation progressed, social and cultural values altered and advances in medicine fundamentally transformed understanding of disease. But his canvas is even broader and he takes account of matters such as the influence of the geography of America and the extraordinary vitality and courage of the pioneers of that great country.

There are many fascinating insights. An example concerns the conception of what constituted 'minor surgery' at that time. We are informed that, as late as 1885, procedures such as amputations of the fingers and toes, and operations on the eye and on the anus were regarded as too minor to warrant anaesthetisation for their performance.

Some notions, conventional to the European, may need to be reconsidered in the light of the evidence presented here. In a thoughtful analysis of contemporary records, the belief (in America at least) that the use of anaesthesia to make possible an increasing number of operations led to an increase in death rate, as a result of infection and shock, is challenged. The author appraises the influence on death rate of the increase in the numbers of accidents associated with the inexorable march forward of industrialisation, and of the extension of surgery to patients earlier considered for various reasons—gender, age, social class, for example—unsuitable for anaesthetics. These perceptions introduce questions about the validity of the more 'obvious' explanations for increase in the death rate.

Again, did the need for surgery for the great numbers of casualties of the mid-century wars make for a readier acceptance of anaesthesia in America or, indeed, in Europe? The answer may prove to be in the affirmative, but to a lesser extent than some of us hitherto thought.

There is so much of interest and importance to be found in this distinguished work that few students of the roots of our specialty, or of medical history in general, could fail to derive pleasure, gain knowledge or find food for rumination. Some idea of the breadth and depth of Mr Pernick's work is conveyed by the fact that the appendices, the notes relevant to each page of text and the very extensive and broad bibliography, in all, amount to some 150 pages.

This study of how profoundly the discovery of anaesthetics affected the profession and its patients in nineteenth century Britain would be valuable in itself and might well unearth a very different story.

J.E. Riding

Care of the Postoperative Surgical Patient

Edited by J.A.R. Smith and J. Watkins. Pp. 273, Butterworth and Co., 1985. £33.

This is a collection of sixteen interesting essays edited by a scientific immunologist and an ex-academic general surgeon. The immediate link between the two editors is location: they both work in Sheffield, but the sustained link, apart from their well-known excellence in their own fields, must be an interest in the postoperative period. There are not many books on this subject and very few (possibly none) which consider the matters from so many different view points. One, therefore, read with considerable anticipation and interest.

The book is divided, presumably related to the title, into five parts: immediate problems, fluid requirements, cardiovascular and pulmonary complications, infection and special situations. Each of the chapters deals with one subject, there is a little overlap and each author is commendably brief. The illustrations, tables, references and index are satisfactory.

Clichés abound in book reviews written by those who try not only to be objective but also, at the same time, inoffensive and literary. For example, there is the ecclesiastical-shell-covered-ovum phrase, which is sometimes used about books to indicate that were a histogram of value/interest/relevance to be plotted against chapter number it would have a saw-toothed shape. That description fits this book. Peaks are the chapters by Charlton, Bax and Woods, and Woodcock and Ledingham. Charlton, because he presents a characteristically forthright criticism of the current management of postoperative pain followed by a critical review of the literature on the newer analgesics and of the newer pharmaceutics of older analgesics. Bax and Woods, because they address the problem of interactions between many of the factors, which are important in the postoperative period and which are concerned with drug action, in a realistic and comprehensible manner. Woodcock and Ledingham, because they write clearly about a subject of which they have considerable clinical experience: the respiratory complications of sepsis.

There are troughs which will be apparent to the individual reader; their identity will, one suspects, depend on the specialty of the reader, but they are not confined to one discipline. The readership should be composed of post diploma anaesthetists and surgeons and the book should be available in postgraduate libraries for them to read. There are a number of useful references, not only if you are about to operate in a hyperbaric chamber (special situations), but also if you are concerned about matters more mundane and relevant to the everyday care of patients.

J.N. Lunn

Opioids in Anaesthesia

Edited by F.G. Estafanous. Pp. 318, Butterworth Publishers, 1985. £42.00 (hard cover).

This book is the product of a two day symposium organised by the Cleveland Clinic Foundation in 1983. It comprises eight sections, each containing a number of chapters, covering the following topics: backgrounds and concepts, composition, action and physiological effects, ultra-short acting opioids, short acting opioids, cardiovascular effects of opioid anaesthesia, use of opioids in cardiac anaesthesia, adjuvants to opioid anaesthesia and opioid anaesthesia and postoperative care. There are 79 contributing authors and a number of additional participants who contribute to the discussion at the end of the sections.

Transposition of the spoken to the written word is difficult and the editor is to be congratulated on performing this task well. The text is nicely laid out and readable, and the illustrations, although few, are very clear. The shortness of some of the chapters, however, would indicate that there was some difficulty in persuading all the contributors to deliver their manuscripts on time. The disappointment in the book is really the contents, as most have concentrated on three drugs (fentanyl, alfentanil and sufentanil), their cardiovascular effects and use in cardiac anaesthesia; the literature is already bulging with such information. As a result there is a considerable amount of repetition, e.g. 'Opioid Anesthesia for Valve Surgery' is followed by 'The Value of Opioids in Valve Replacement Procedures'. Opioid 'anaesthesia' obviously generates much emotion amongst those who practise this extraordinary technique, as judged by the discussions, and it was a joy to read Chapter 32 by Roizen, who concluded '... that no data justify the belief that any narcotic or inhalational agent is superior in its effects on outcome when used for cardiac or vascular anaesthesia'.

What an opportunity was missed to bring experts together to discuss the newest use of opioids in anaesthesia, namely their direct spinal application. The time is ripe for such a meeting and yet it is only considered in three of the 53 chapters. This, therefore, is neither a book for the ordinary practising anaesthetist, nor indeed for departmental libraries, but would be valuable to those particularly interested in high dose opioids and their cardiovascular effects and who are prepared to be separated from £42 to own it.

M. Morgan

600 MCQs in Anaesthesia: Basic Sciences

P.J. Simpson and N.W. Goodman. Pp. 244, Churchill Livingstone, 1985. £7.95.

The title describes this book accurately! It starts with an introduction which states clearly the purpose of multiple choice questions in general and that of this book. These questions in the FFARCS examinations are designed to test basic knowledge are not meant to confuse; this book has the same purposes. Students are warned in the preface against trying to argue the toss with the authors and, one supposes, this advice is directed to book reviewers as well. There are ten sets of questions, as papers, on many subjects. There is rather more physics and measurement than one would have anticipated but otherwise there seems to be a suitable mix. The discipline of private attempts at completion is both rewarding and revealing! The authors are to be congratulated; their book will stimulate and enlighten.

J.N. Lunn

Anaesthesia, 1986, Volume 41, pages 229–230

Audiovisual reviews

Nursing aspects of central venous pressure lines 229
Graves Medical Audiovisual Library (VHS/Beta videocassette)
Management of the adult respiratory distress syndrome 229
Oxford Educational Resources Ltd (Umatic videocassette)
Clinical Physics and Measurement for Anaesthetists 230
Oxford Educational Resources Ltd (Tapeslide lectures)

Nursing Aspects of Central Venous Pressure Lines

By J.V. Daws (*Kent and Canterbury Hospital*). VHS/Beta videocassette. Colour. Buy from Graves Medical Audiovisual Library, Holly House, 22 New London Road, Chelmsford, CM2 9BJ. Ref. GVC 22VE/BE. 15 minutes. (1984).

This is a tapeslide presentation converted to video and is concerned with the nurse's role in measuring central venous pressure (CVP). It is a simple presentation, outlining what a CVP measurement is, how the line is inserted and the various sites that can be used. It also shows the types of catheters used, how actually to measure a CVP with the correct positioning of the patient and the zeroing of the measuring scale.

The method used to illustrate the insertion of the CVP line could have been better defined. The Seldinger technique was illustrated, but the role of the guide wire was somewhat confused. The author states that two nurses are required to scrub up in order to change the giving set and tubing—a procedure which is carried out every day. This would mean that a third nurse would have to open up packs, which would not make this a cost-effective exercise and I think is an unnecessary use of resources.

The description of measuring the CVP was clearly and simply described. Some nurses are confused, when measuring CVPs, about the zero of the manometer and about the 3-way tap. This is clearly explained and illustrated and upper and lower limits of CVP measurements are given.

The circumstances for more frequent recording or no recording at all are not mentioned. For example, if there is a sudden change in the patient's clinical condition then the CVP should be recorded more frequently. On the other hand, the CVP should not be recorded during coughing and the measurement is inaccurate when the filter at the top of the manometer column is wet.

This is a useful item if it is used in conjunction with a practical demonstration for nurses of all grades.

S. Boyle

Management of the Adult Respiratory Distress Syndrome

By D.R. Dantzker (*University of Michigan*). Umatic videocassette. Colour. Buy from Oxford Educational Resources Ltd., 197 Botley Road Oxford, OX2 0HE. 30 minutes. (1982).

This video presentation consists of a conversation on the topic of adult respiratory distress syndrome, illustrated with a number of static diagrams. The programme is accompanied by a small booklet with multiple choice questions based on the material covered.

The principal speaker gives a spirited account of the adult respiratory distress syndrome, covering those aspects of the pathophysiology which are useful in understanding the treatment offered, namely oxygen and its effects, artificial ventilation, positive end expiratory pressure, fluid management and inotropic support. The explanations given are succinct and, as of the date of publication of the video, up to the minute, although it should be noted that this was first published in 1982. The presentation goes along at a fairly brisk rate and the principal author gives an impression of great enthusiasm for his subject, unhampered by the fact that in the video he is lecturing with his left arm in a heavy plaster cast. The decision to use only static diagrams is perhaps a little disappointing with the video medium; however, the selection of the diagrams for use is good and they adequately illustrate the author's comments.

On the whole, this is a most worthwhile presentation and trainees in anaesthesia would derive considerable benefit from watching it, as would any others whose work may bring them to manage patients suffering from this distressing and intractable disorder.

Potential users should note that the recording is made on American colour standard and an N.S.T.C. recording machine and monitor are both necessary to view this production in colour.

W.G. ANDERSON

Clinical Physics and Measurement for Anaesthetists

By G.D. PARBROOK, P.D. DAVIS AND E.O. PARBROOK (*Royal Infirmary, Glasgow*). Tapeslide lectures. But or hire from Oxford Educational Resources Ltd., 197 Botley Road, Oxford, OX2 0HE. (1985).

New editions of the following 7 programmes are now available:

Flow 2—Measurement and Injectors
Diffusion and Osmosis
Electrical Safety
Blood Pressure Measurement 1—Non invasive techniques
Blood Pressure Measurement 2—Invasive Techniques
Gas Chromatography
Oxygen Measurement 1

Anaesthesia, 1986, Volume 41, pages 231

Index of computer programs

21.2.14

Author E.C. Bloch (Department of Anesthesiology, Duke University Medical Center, Durham, North Carolina 27710 U.S.A.).

Title A Computer Generated Guide for Paediatric Anaesthesia.

Description The program is designed to calculate and provide individualised data for use during the administration of anaesthesia to paediatric patients. It provides guidelines for tracheal tube size, fresh gas flowrates for the Mapleson D System, initial and incremental dosages of drugs, fluid administration and blood replacement, and anticipated urinary losses. The operator may select a worksheet for neonates, or one for infants and children up to 30 kg body weight. It also provides resuscitation drug doses for bolus and/or infusion administration if requested by the operator. Required variables for input are the patients name, age, weight, haematocrit, and hours NPO.

The purposes of the program is to provide a quick simple and clear individualised printout to guide the anaesthetist and to avoid potentially disastrous miscalculations.

Languages Applesoft Basic, Advanced Basic (IBM MS DOS 2.0 or higher), Radio Shack Basic (tape cassette).

Computing Facility Apple II C, IBM PC, Radio Shack TRS 80 model PC2 (tape cassette).

24.1.24

Author A.J. Matthews (Department of Anaesthesia, Sunderland District General Hospital).

Title Neonatal Total Parenteral Nutrition.

Description This program is designed to be used on a neonatal intensive care unit for prescription of total parenteral nutrition. Information requested is the baby's weight (kg), daily fluid intake requirement (ml/kg/day), dextrose strength (%), lipid and Vamin requirements (g/kg/day), sodium, potassium, calcium and magnesium requirements (mmol/kg/day) and composition and volume (ml/day) of two other infusions. An aminophylline in glucose infusion can also be used (for treatment of neonatal apnoeas) and an input of mg/kg/hour is required for that.

From these data the program calculates a complete menu for total parenteral nutrition based on Intralipid 20%, Vamin glucose and glucose with added electrolytes, trace elements and vitamins. It also calculates the dilution of aminophylline required, the calorie intake (kcal/kg/day) and glucose intake (mg/kg/minute).

Language Sinclair Basic.

Computing Facility Sinclair Spectrum (tape version).

25.1.32

Author J.N. Horton (Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW).

Title Multiple Choice Questionnaire (MCQ) Marker.

Description Up to 300 candidates' responses to practice MCQs of the 'stem-and-5-branch' type can be input and each candidate's individual question and total scores calculated and displayed. The computer is not used to present or answer the questions, although the program could fairly readily be incorporated into an existing 'self-test' program. The program will also 'validate' each question for its ability to discriminate between good and bad candidates, based on their total scores.

Language BBC Basic.

Computing Facility BBC model B with compatible printer, disk or cassette.

Details of programs to be included in this catalogue should be sent to Dr M.J. Harrison, Department of Anaesthesia, C Floor, East Block, University Hospital and Medical School, Clifton Boulevard, Nottingham NG7 2UH. They should be of relevance to anaesthesia or intensive care. Programs that involve the application of the basic sciences, will also be accepted.

Further details of the programs can be obtained from the department or person directly involved.

Anaesthesia, 1986, Volume 41, pages 232–240

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for August 1985. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Abdominal surgery

Mucosal damage in *Escherichia coli* sepsis. Arvidsson, S., Falt, K. *et al. Circulatory Shock* 1985; **16:** 383.

Intestinal ischaemia. Gillespie, I.E. *Gut* 1985; **26:** 653.

Control of intestinal absorption by the renin-angiotension system. Levens, N.R. *American Journal of Physiology* 1985; **249:** G3.

Nonhomogeneous redistribution of mesenteric blood flow after tolazoline during group B streptococcal sepsis in piglets. Meadow, W.L., Meus, P.F. *Developmental Pharmacology and Therapeutics* 1985; **8:** 209.

First experimental results with the oxygen electrode as a local blood flow sensor in canine colon. Piasecki, C. *British Journal of Surgery* 1985; **72:** 452.

Pharmacology

Adrenergic drugs and their antagonists

Recurring cardiac myxoma. Gray, I.R., Williams, W.G. *British Heart Journal* 1985; **53:** 645.

Labetalol infusion in hypertensive emergencies. Lebel, M., Langlois, S. *et al. Clinical Pharmacology and Therapeutics* 1985; **37:** 615.

Effects of clonidine on blood pressure, noradrenaline, cortisol, growth hormone and prolactin plasma levels in high and low intestinal tone depressed patients. Lechin, F., Dijs, B. Van Der. *Neuroendocrinology* 1985; **41:** 156.

Serum myoglobin concentrations are decreased by beta-adrenergic stimulation. Ljunghall, S., Roxin, L.E. *et al. European Journal of Applied Physiology* 1985; **54:** 54.

Serum creatine phosphokinase levels during treatment with beta-adrenoceptor blocking agents. Saruta, T., Suzuki H. *Journal of Cardiovascular Pharmacology* 1985; **7:** 805.

Role of dopamine in the neurotoxic effects of methamphetamine. Schmidt, C.J., Ritter, J.K. *et al. Journal of Pharmacology and Experimental Therapeutics* 1985; **233:** 539.

Use of intravenous regional sympathetic block in upper limb angiography. Vaughan, R.S., Lawrie, B.W., Sykes, P.J. *Annals of the Royal College of Surgeons of England* 1985; **67:** 309.

y-L-glutamyl-L-dopa is a dopamine pro drug, relatively specific for the kidney in normal subjects. Worth, D.P., Harvey, J. *et al. Clinical Science* 1985; **69:** 207.

Anaesthetic agents

Prolongation of thiopentone-induced sleep by trazodone and its metabolite, m-chlorophenylpiperazine. Adamus A., Sansone M. *et al. Journal of Pharmacy and Pharmacology* 1985; **37:** 504.

Comparative metabolic effects of halothane and enflurane in rat heart cell culture. Albrecht, R.F., Miletich, D.J., Dinsmore, P. *Journal of Cardiovascular Pharmacology* 1985; **7:** 799.

Effect of parenterally administered atropine on the percutaneous absorption of phencyclidine and methadone. Bailey, D.N., Briggs, J.R., Coffee, J.J. *Life Sciences* 1985; **37:** 417.

Evaluation of infusion regimens for thiopentone as a primary anaesthetic agent. Crankshaw, D.P., Edwards, N.E. *et al. European Journal of Clinical Pharmacology* 1985; **28:** 543.

Effects of anesthetic agents on bile pigment excretion in the rat. Gourley, G.R., Mogilevsky, W. *et al. Hepatology* 1985; **5:** 610.

Species differences in response to trichloroethylene. II. Biotransformation in rats and mice. Green, T., Prout, M.S. *Toxicology and Applied Pharmacology* 1985; **79:** 401.

Integrated pharmacokinetics and pharmacodynamics of atropine in healthy humans. 2. Pharmacodynamics. Hinderling, P.H., Gundert-Remy, U. *et al. Journal of Pharmaceutical Science* 1985; **74:** 711.

Integrated pharmacokinetics and pharmacodynamics of atropine in healthy humans. 1. Pharmacokinetics. Hinderling, P.H., Gundert-Remy, U. *et al. Journal*

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London, WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. An exact copy of the monthly section or various cumulative classifications of the Anaesthetic Literature published in the Journal can be obtained on application to him. References from January 1984 have been entered on data base and search facilities are also available. All communications about this matter should be addressed to Dr Kaufman please.

of Pharmaceutical and Therapeutics 1985; **74:** 703.

Atropine serum concentration after multiple inhaled doses of atropine sulfate. Kradjan, W.A., Smallridge, R.C. *et al. Clinical Pharmacology and Theraputics* 1985; **38:** 12.

Ether cystitis. Nellans, R.E., Ellis, L.R., Kenny, *Journal of the American Medical Association* 1985; **254:** 530.

Species differences in response to trichloroethylene. I. Pharmacokinetics in rats and mice. Prout, M.S., Provan, W.M., Green, T. *Toxicology and Applied Pharmacology* 1985; **79:** 389.

Hemodynamic and respiratory effects of dezocine, ciramadol, and morphine. Rothard, R.L., Schreiner, B.F., Yu, P.N. *Clinical Pharmacology Therapeutics* 1985; **38:** 84.

Analgesic agents

Multiple sites for the cardiovascular actions of fentanyl in rats. Gautret, B., Schmitt, H. *Journal of Cardiovascular Pharmacology* 1985; **7:** 649.

Chronic stress, aging and morphine analgesia—chronic stress affects the reactivity to morphine in young mature but not old rats. Giradot, M.N., Holloway, F.A. *Journal of Pharmacology and Experimental Therapeutics* 1985; **233:** 545.

Ranitidine does not alter pethidine disposition in man. Guay, D.R.P., Meatherall, R.C. *et al. British Journal of Clinical Pharmacology* 1985; **20:** 55.

Muscle relaxants

Atracurium-receptor kinetics: simple behavior from a mixture. Amaki, Y., Waud, B., Waud, D.R. *Anesthesia and Analgesia* 1985; **64:** 777.

Anti-acetycholine receptor antibody titer with extended thymectomy in myasthenia gravis. Kagotani, K., Monden, Y. *et al. Journal of Thoracic and Cardiovascular Surgery* 1985; **90:** 7.

Intracellular ionized calcium concentration in muscles from humans with malignant hyperthermia. Lopez, J.R., Alamao, L. *et al. Muscle and Nerve* 1985; **8:** 355.

The effect of acid-base balance on fatigue of skeletal muscle. Mainwood, G.W., Renaud, J.M. *Canadian Journal of Physiology and Pharmacology* 1985; **63:** 403.

Measurement of junctional acetylcholine receptors in myasthenia gravis: clinical correlates. Pestronk, A., Drachman, D.B., Self, S.G. *Muscle and Nerve* 1985; **8:** 245.

Edrophonium: a useful provocative test for esophageal chest pain. Richter, J.E., Hackshaw, B.T. *et al. Annals of Internal Medicine* 1985; **103:** 14.

A comparison of physostigmine and soman using taste aversion and nociception. Romano, J.A., King, J.M., Penetar, D.M. *Neurobehavioral Toxicology and Teratology* 1985; **7:** 243.

Neuromuscular effects of atracurium during halothane–nitrous oxide and enflurane–nitrous oxide anesthesia in humans. Rupp, S.M., McChristin, J.W., Miller, R.D. *Anesthesiology* 1985; **63:** 16.

Atracurium—clinical strategies for preventing histamine release and attenuating the haemodynamic response. Savarese, J.J., Basta, S.J. *et al. British Journal of Anaesthesia* 1985; **57:** 550.

Interaction among agents that block end-plate depolarization competitively. Waud, B.E., Waud, D.R. *Anesthesiology* 1985; **63:** 4.

Fatigue trends in and the diagnosis of myasthenia gravis by frequency analysis of EMG interference patterns. Yaar, I., Mitz, A.R., Pottala, E.W. *Muscle and Nerve* 1985; **8:** 328.

Other drugs

Mechanism of action of sodium cromoglycate. Biggs, D.F., Goel, V. *Canadian Journal of Physiology and Pharmacology* 1985; **63:** 760.

Cimetidine interaction with liver microsomes *in vitro* and *in vivo*. Involvement of an activated complex with cytochrome P-450. Jensen, J.C., Gugler, P. *Biochemical Pharmacology* 1985; **34:** 2141.

Midazolam kinetics before, during and after cardiopulmonary bypass surgery. Kanto, J., Himberg, J.J. *et al. International Journal of Clinical Pharmacology Research* 1985; **5:** 123.

Complications

Propylene glycol-induced heparin resistance during nitroglycerin infusion. Col, J., Col-Debeys, C. *et al. American Heart Journal* 1985; **110:** 171.

Hypercapnia during weaning: a complication of nutritional support. Dark, D.S., Pingleton, S.K., Kerby, G.R. *Chest* 1985; **88:** 141.

Ischaemic brain. Dearden, N.M. *Lancet* 1985; **2:** 255.

Neuromuscular disorders associated with D-penicillamine treatment for rheumatoid arthritis. Devogelaer, J.P., Isaac, G. *et al. International Journal of Clinical Pharmacology Research* 1985; **5:** 143.

Nocturnal oxyhemoglobin desaturation following tracheostomy for obstructive sleep apnea. Fletcher, E.C., Brown, D.L. *American Journal of Medicine* 1985; **79:** 35.

Rapid development of obstructive sleep apnea following hemidiaphragmatic and unilateral vocal cord paralysis as a complication of mediastinal surgery. Hoffstein, V., Taylor, R. *Chest* 1985; **88:** 145.

Protamine-induced fatal anaphylaxis—prevalence of antiprotamine immunoglobulin-E antibody. Sharath, M.D., Metzger, W.J. *et al. Journal of Thoracic and Cardiovascular Surgery* 1985; **90:** 86.

Apparatus

Arterial blood gas measurement. Burki, N.K. *Chest* 1985; **88:** 3.

Contamination of internal jugular cannulae. Clayton, D.G., Shanahan, E.C. *et al. Anaesthesia* 1985; **40:** 523.

Anaesthetic breathing systems. Conway, C.M. *British Journal of Anaesthesia* 1985; **57:** 649.

Pressure-flow relationships of endotracheal tubes during high-frequency ventilation. Gavriely, N., Solway, J. *et al. Journal of Applied Physiology* 1985; **59:** 3.

Arterial micropuncture. An advance in blood-gas analysis. Harnoncourt, K., Marsoner, H., Forche, G. *Respiration* 1985; **48:** 67.

Paediatric anaesthetic equipment. Hatch, D.J. *British Journal of Anaesthesia* 1985; **57:** 672.

Quantitative analysis of common anaesthetic agents. Heusler, H. *Journal of Chromatography* 1985; **340:** 273.

Warming blood before transfusion. Does immersion warming change blood composition. Marks, R.J., Minty, B.D., White, D.C. *Anaesthesia* 1985; **40:** 541.

Vaporization and vaporizers. White, D.C. *British Journal of Anaesthesia* 1985; **57:** 658.

General anaesthetic procedures

The normalization of sleep after surgical procedures, with and without the use of a hypnotic benzodiazepine. Bischoff, R.C., Schratzer, M., Anders, A. *Current Therapeutic Research* 1985; **38:** 3.

Pronounced episodic oxygen desaturation in the post-operative period: its association with ventilatory pattern and analgesic regimen. Catley, D.M., Thornton, C. *et al. Anesthesiology* 1985; **63:** 20.

Effect of alfentanil anaesthesia on the adrenocortical and hyperglycaemic response to abdominal surgery. Moller, I.W., Krantz, T. *et al. British Journal of Anaesthesia* 1985; **57:** 591.

Posterior spinal fusion and instrumentation in the treatment of adolescent idiopathic scoliosis. Youngman, P.M.E., Edgar, M.A. *Annals of the Royal College of Surgeons of England* 1985; **67:** 313.

General interest

Phaeochromocytoma of broad ligament. Case report. Al-Jafari, M.S., Panton, H.M., Gradwell, E. *British Journal of Obstetrics and Gynaecology* 1985; **92:** 649.

Pheochromocytoma of the organ on Zuckerkandl presenting as shock. Ciobotaru, M., Eisenman, A. *et al. Israel Journal of Medical Sciences* 1985; **21:** 517.

Local analgesia

Leaves and needles: the introduction of surgical local anesthesia. Fink, B.R. *Anesthesiology* 1985; **63:** 77.

Spinal and epidural analgesia

Opioid peptides and their receptors. Kosterlitz, H.W. *Proceedings of the Royal Society of London. Series B-Biological Sciences* 1985; **225:** 27.

Spinal opioids

Epidural morphine: a clinical double-blind study of dosage. Lanz, E., Kehrberger, E., Theiss, D. *Anesthesia and Analgesia* 1985; **64:** 786.

Enkephalin and substance P dynamics studied in morphine addiction and potential respiratory failure. Bergstrom, L. *Acta Pharmaceutica Suedica* 1985; **22:** 112.

Plasma corticosterone changes in response to central or peripheral administration of kappa-opiate and sigma-opiate agonists. Eisenberg, R.M. *Journal of Pharmacology and Experimental Therapeutics* 1985; **233:** 863.

Infusion of opiates into substantia nigra protects against maximal electroshock seizures in rats. Garant, D.S., Gale, K. *Journal of Pharmacology and Experimental Therapeutics* 1985; **234:** 45.

Analgesia and autonomic function following intrathecal administration of morphine and norepinephrine to the rat. Loomis, C.W., Cervenko, F.W. *et al. Canadian Journal of Physiology and Pharmacology* 1985; **63:** 656.

Sigma-opioid receptor—characterization and co-identity with the phencyclidine receptor. Mendelsohn, I.G., Kalra, V. *et al. Journal of Pharmacology and Experimental Therapeutics* 1985; **233:** 587.

In vivo receptor binding of opioid drugs at the mu-site. Rosenbaum, J.S., Holford, N.H., Sadee, W. *Journal of Pharmacology and Experimental Therapeutics* 1985; **233:** 735.

Obstetric anaesthesia and analgesia

Intravenous prostacyclin in the management of pregnancies complicated by severe hypertension. Belch, J.J.F., Thorburn, J. *et al. Clinical and Experimental Hypertension Part B—Hypertension in Pregnancy* 1985; **4:** 75.

Maternal deaths in Washington State. Benedetti, T.J., Starzyk, P., Frost, F. *Obstetrics and Gynecology* 1985; **66:** 99.

Experience with the pulmonary artery catheter in obstetrics and gynecology. Clark, S.L., Horenstein, J.M. *et al. American Journal of Obstetrics and Gynecology* 1985; **152:** 374.

Management of burns in pregnant women. Deitch, E.A., Rightmire, D.A. *et al. Surgery Gynecology and Obstetrics* 1985; **161:** 1.

A return to maternal mortality studies: a necessary effort. Fox, L.P. *American Journal of Obstetrics and Gynecology* 1985; **152:** 379.

Effects of caffeine ingestion during pregnancy. Furuhasi, N., Sato, S. *et al. Gynecologic and Obstetric Investigation* 1985; **19:** 187.

Obstetric outcome in women with epilepsy. Hiilesmaa, V.K., Bardy, A., Teramo, K. *American Journal of Obstetrics and Gynecology* 1985; **152:** 499.

Pregnancy-induced increase in metoprolol metabolism. Hoogstedt, S., Lindberg, B. *et al. Clinical Pharmacology and Therapeutics* 1985; **37:** 688.

Arginine vasopressin in amniotic fluid, arterial and venous cord plasma and maternal venous plasma. Johannesen, P., Pedersen, E.B. *et al. Gynecologic and Obstetric Investigation* 1985; **19:** 192.

Plasma catecholamines and modes of delivery: relation between catecholamine levels/platelet aggregation and adrenoceptor radioligand binding. Jones, C.R., McCullouch, J. *et al. British Journal of Obstetrics and Gynaecology* 1985; **92:** 593.

Current concepts: acute fatty liver of pregnancy. Kaplan, M.M. *New England Journal of Medicine* 1985; **313:** 367.

Effect of metoprolol in combination with hydralazine on fetal heart rate patterns during hypertensive pregnancy and delivery. Lindeberg, S., Oxelsson, O. *et al. Clinical and Experimental Hypertension. Part B—Hypertension in Pregnancy* 1985; **4:** 87.

Water metabolism and vasopressin secretion in pregnancy. Lindheimer, M.D., Barron, W.M., Davison, J.M. *Vasopressin.* R.W. Schrier. (Ed), Raven Press (New York), 1985: p. 229.

Immune complexes in preeclampsia and normal pregnancy. Massobrio, M., Benedetto, C. *et al. American Journal of Obstetrics and Gynecology* 1985; **152:** 578.

Evaluation of the use of continuous lumbar epidural anesthesia for hypertensive pregnant women in labour. Moore, T.R., Key, T.C. *et al. American Journal of Obstetrics and Gynecology* 1985; **152:** 404.

Current concepts: management of medical problems in pregnancy—severe cardiac disease. Sullivan, J.M., Ramanathan, K.B. *New England Journal of Medicine* 1985; **313:** 304.

A comparative oral analgesic study of indoprofen, aspirin, and placebo in postpartum pain. Sunshine, A., Zighelboim, I. *et al. Journal of Clinical Pharmacology* 1985; **25:** 374.

Hypertension in pregnancy—long-term effects on blood pressure in mothers and children. Svensson, A. *Acta Medica Scandinavica* 1985; Suppl 695: 5.

Catecholamine responses to changes in posture during human pregnancy. Whittaker, P.G., Gerard, J., Lind, T. *British Journal of Obstetrics and Gynaecology* 1985; **92:** 586.

Paediatric anaesthesia and intensive care

Sleep apnoea profile in preterm infants recovering from respiratory distress syndrome. Bentele, K.H.P., Albani, M. *et al. Archives of Disease in Childhood* 1985; **60:** 547.

Unexplained deaths in a children's hospital: an epidemiologic assessment. Buehler, J.W., Smith, L.F. *et al. New England Journal of Medicine* 1985; **313:** 211.

Commentary. Enquiry into perinatal death. Chalmers, I. *British Journal of Obstetrics* 1985; **92:** 545.

Ventilatory responses of children to changes in deadspace volume—studies using the T-piece (mapleson-F) system. Charlton, A.J., Lindahl, S.G.E., Hatch, D.J. *British Journal of Anaesthesia* 1985; **57:** 562.

Cerebral cortical function in infants at risk for sudden infant death syndrome. Clancy, R.R., Spitzer, A.R. *Annals of Neurology* 1985; **18:** 41.

Ventilatory control and carbon dioxide response in preterm infants with idiopathic apnea. Durand, M., Cabal, L.A. *et al. American Journal of Diseases of Children* 1985; **139:** 717.

Catecholamine response to chest physiotherapy and endotracheal suctioning in preterm infants. Greisen, G., Frederiksen, P.S. *et al. Acta Paediatrica Scandinavica* 1985; **74:** 525.

Pathophysiological analysis of hypoxaemia during acute severe asthma. Hori, T. *Archives of Disease in Childhood* 1985; **60:** 640.

A mysterious cluster of deaths and cardiopulmonary arrests in a pediatric intensive care unit. Istre, G.R., Gustafson, T.L. *et al. New England Journal of Medicine* 1985; **313:** 205.

Drug-electrophysiology studies in infants, children and adolescents. Kugler, J.D., Bansal, A.M. *et al. American Heart Journal* 1985; **110:** 144.

Biphasic response of respiratory frequency to hypercapnea in preterm infants. Martin, R.J., Carlo, W.A. *et al. Pediatric Research* 1985; **19:** 791.

Changes in ventilatory patterns during halothane anaesthesia in children. Murat, I., Delleur, M.M. *et al. British Journal of Anaesthesia* 1985; **57:** 569.

Normal plasma-urine osmolality relationship in preterm infants on positive pressure mechanical ventilation. Sujov, P., Seltzer, M., Hochberg, Z. *Acta Paediatrica Scandinavica* 1985; **74:** 601.

Conventional vs high-frequency jet ventilation in piglet model of meconium aspiration—comparison of pulmonary and hemodynamic effect. Trindade, O., Goldberg, R.N. *et al. Journal of Pediatrics* 1985; **107:** 115.

Cardiac output in infants of insulin-dependent diabetic mothers. Walther, F.J., Siassi, B. *et al. Journal of Pediatrics* 1985; **107:** 109.

Two controlled trials of dry artificial surfactant: early effects and later outcome in babies with surfactant deficiency. Wilkinson, A., Jenkins, P., Jeffrey, J. *Lancet* 1985; **2:** 287.

Renal response to frusemide in preterm infants with respiratory distress syndrome during the first three postnatal days. Yeh, T.F., Raval, D. *et al. Archives of Disease in Childhood* 1985; **60:** 621.

Treatment and medication

Septic complications of corticosteroid administration after central nervous system. Demaria, E.J., Reichman, W. *et al. Annals of Surgery* 1985; **202:** 248.

Effects of therapeutic intervention on the metabolic responses to injury. Fellows, I.W., Woolfson, A.M.J. *British Medical Bulletin* 1985; **41:** 287.

Acute vasoconstrictor response to intravenous furosemide in patients with chronic congestive heart failure: activation of the neurohumoral axis. Francis, G.S., Siegel, R.M. *et al. Annals of Internal Medicine* 1985; **103:** 206.

Intensive insulin therapy reduces counterregulatory hormone responses to hypoglycemia in patients with type I diabetes. Simonson, D.C., Tamborlane, W.V. *et al. Annals of Internal Medicine* 1985; **103:** 184.

Long-term prognosis after myocardial infarction in men with diabetes. Ulvenstam, G., Aberg, A. *et al. Diabetes* 1985; **34:** 787.

Cardiovascular system

Physiology

Respiratory and cardiovascular responses to hyperoxia, hypoxia and hypercapnia in the renal hypertensive rabbit: role of carotid body chemoreceptors. Angell-James, J.E., Clarke, J.A. *et al. Journal of Hypertension* 1985; **3:** 213.

Haemostatic response to trauma. Bennett, B., Towler, H.M.A. *British Medical Bulletin* 1985; **41:** 274.

Patients with malignant or potentially malignant ventricular arrhythmias: opportunities and limitations of drug therapy in prevention of sudden death. Bigger, J.T. *Journal of the American College of Cardiology* 1985; **5:** 23B.

Factors relating to the development of hypertension after cardiopulmonary bypass. Cooper, T.J., Clutton-Brock, T.H. *et al. British Heart Journal* 1985; **54:** 91.

Clinical electrophysiology and electrocardiography. Role of the electrocardiogram in identifying the patient at increased risk for sudden death. Fisch, C. *Journal of the American College of Cardiology* 1985; **5:** 6B.

Mitral valve prolapse. Jeresaty, R.M. *Journal of the American Medical Association* 1985; **254:** 793.

Ischaemic heart disease and prodromes of sudden cardiac death: is it possible to identify high risk groups for sudden cardiac death? Madsen, J.K. *British Heart Journal* 1985; **54:** 27.

Mechanisms of neurogenic pulmonary edema. Malik, A.B. *Circulation Research* 1985; **57:** 1.

Reflex cardiovascular regulation in humans. Mancia, G., Grassi, G. *et al. Journal of Cardiovascular Pharmacology* 1985; **7:** S152.

The effect of cardiac autonomic blockade on ventricular response to changes in preload. Raven, P.B., Klein, K. *et al. Journal of the Autonomic Nervous System* 1985; **13:** 263.

Electrophysiologic testing in patients at high risk for sudden cardiac death. Spielman, S.R., Greenspan, A.M. *et al. Journal of the American College of Cardiology* 1985; **6:** 31.

On the mechanisms underlying cardiac standstill: factors determining success or failure of escape pacemakers in the heart. Vassalle, M. *Journal of the American College of Cardiology* 1985; **5:** 35B.

Treatment and medication

Pharmacology of nitroglycerin and long-acting nitrates. Abrams, J. *American Journal of Cardiology* 1985; **56:** 12A.

Effects of amrinone on myocardial energetics in severe congestive heart failure. Baim, D.S. *American Journal of Cardiology* 1985; **56:** 16B.

Prevention of gram-negative shock and death in surgical patients by antibody to endotoxic core glycolipid. Baumgartner, J.D., Glauser, M.P. *et al. Lancet* 1985; **2:** 59.

Captopril potentiates chronotropic baroreflex responses to carotid stimuli in humans. Ebert, T.J. *Hypertension* 1985; **7:** 602.

Effects of prostacyclin infusion on renal function during cardiopulmonary bypass. Fedderson, K., Aren, C. *et al. Annals of Thoracic Surgery* 1985; **40:** 16.

Guanadrel: a review of its pharmacodynamic and pharmacodynamic and pharmacokinetic properties and therapeutic efficacy in hypertension. Finnerty, jr. F.A., Brogden, R.N. *Drugs* 1985; **30:** 22.

Cardioselective and nonselective beta-adrenoceptor blocking drugs in hypertension. Floras, J.S., Hassan, M.O. *et al. Journal of the American College of Cardiology* 1985; **6:** 186.

The metabolism and pharmacokinetics of nicardipine hydrochloride in man. Graham, D.J.M., Dow, R.J. *et al. British Journal of Clinical Pharmacology* 1985; **20:** S23.

Blood transfusion and surgery. Horsey, P.J. *British Medical Journal* 1985; **291:** 234.

Captopril-induced renal insufficiency and the role of sodium balance. Hricik, D.E. *Annals of Internal Medicine* 1985; **103:** 222.

Pharmacology of potent and selective S2-secrotonergic antagonists. Janssen, P.A.J. *Journal of Cardiovascular Pharmacology* 1985; **7:** S2 (Suppl 7).

Naloxone potentiates the cardiovascular effects of catecholamines in canine hemorrhagic shock. Lechner, R.B., Gurll, N.J., Reynolds, D.G. *Circulatory Shock* 1985; **16:** 347.

Effect of cimetidine on verapamil disposition. Loi, C.-M., Rollins, D.E. *et al. Clinical Pharmacology and Therapeutics* 1985; **37:** 654.

Intravenous propranolol in the treatment of repetitive ventricular tachyarrhythmias during resuscitation from sudden death. Mason, J.R., Marek, J.C. *et al. American Heart Journal* 1985; **110:** 161.

Effect of hypothermic cardiopulmonary bypass on nitroprusside metabolism. Moore, R.A., Geller, E.A. *et al. Clinical Pharmacology and Therapeutics* 1985; **37:** 680.

Platelet storage for transfusion. Murphy, S. *Seminars in Hematology* 1985; **22:** 165.

Vasodilator therapy for primary pulmonary hypertension: limitations and hazards. Packer, M. *Annals of Internal Medicine* 1985; **103:** 258.

Treatment of ventricular arrhythmia; applications and limitations of noninvasive vs invasive approach. Podrid, P.J. *Chest* 1985; **88:** 121.

Protection against thrombo-embolism. Ruckley, C.V. *British Journal of Surgery* 1985; **72:** 421.

Takayasu's arteritis and its therapy. Shelhamer, J.H., Volkman, D.J. *et al. Annals of Internal Medicine* 1985; **103:** 121.

Measurement of total body water in intensive care patients with fluid overload. Streat, S.J., Beddoe, A.H., Hill, G.L. *Metabolism. Clinical and Experimental* 1985; **34:** 688.

The role of isosorbide dinitrate in the treatment of perioperative hypertension. Thys, D.M., Sivak, G. *et al. American Heart Journal* 1985; **110:** 273.

Pathophysiology of cardiac failure. Weber, K.T., Janicki, J.S., Maskin, C.S. *American Journal of Cardiology* 1985; **56:** 3B.

Respiration

Physiology

The acute effects of intralipid on lung function. Ali, J., Wood, L.D.H. *Journal of Surgical Research* 1985; **38:** 599.

Gas exchange in tidally ventilated and non-steadily perfused lung model. Arieli, R., Farhi, L.E. *Respiration Physiology* 1985; **60:** 295.

Oxygen and the lung, an overview. Barer, G., Wach, R.A. *et al. Pulmonary Circulation in Chronic Lung Disease. Experimental and Clinical Approach. Progress in Respiration Research.* Eds J. Widimsky, J. Herget, J. Mlczoch, S. Karger AG (Basel) 1985; **20:** 1.

Effect of mechanical ventilation with an end-expiratory plateau on gas exchange and haemodynamics in chronic respiratory failure. Battistella, P., Delorme, N. *et al. Clinical Respiratory Failure* 1985; **21:** 243.

Breathing and oxygenation during sleep are similar in normal men and normal women. Catteral, J.R., Calverley, P.M.A. *et al. American Review of Respiratory Disease* 1985; **132:** 86.

Aminophylline reduces hypoxic ventilatory depression—possible role of adenosine. Darnall, R.A. *Pediatric Research* 1985; **19:** 706.

Effects of acid infusion into the esophagus on airflow obstruction and bronchial hyperreactivity in adult asthmatic patients. Denjean, A., Herve, P. *et al. Chest* 1985; **87:** 201S.

The effects of inspiratory resistive training on respiratory muscle function in patients with muscular dystrophy. Dimarco, A.F., Kelling, J.S. *et al. Muscle and Nerve* 1985; **8:** 284.

State-related incidence of spontaneous breathing during high frequency ventilation. England, S.J., Sullivan, C. *et al. Respiration Physiology* 1985; **60:** 357.

Relationship between respiratory muscle electromyogram and rib cage motion in tetraplegia. Estenne, M., Detroyer, A. *American Review of Respiratory Disease* 1985; **132:** 53.

The pathology of asthma. Hogg, J.C. *Chest* 1985; **87:** 152S.

Right ventricular volumes by thermodilution in the adult respiratory distress syndrome. Jardin, F., Gueret, P. *et al. Chest* 1985; **88:** 34.

Oxyhemoglobin saturation during sleep in subjects with and without the obesity-hypoventilation syndrome. Jones, J.B., Wilhoit, S.C. *et al.* Chest 1985; **88:** 9.

Regulation of tissue oxygen extraction is disturbed in adult respiratory distress syndrome. Kariman, K., Burns, S.R. *American Review of Respiratory Disease* 1985; **132:** 109.

Possible function of bronchial surfactant. Lachmann, B. *European Journal of Respiratory Diseases* 1985; **67:** 49.

Regulation of the pulmonary capillary circulation. Lee, G.D. *Pulmonary Circulation in Chronic Lung Diseases. Experimental and Clinical Approach. Progress in Respiration Research.* Eds J. Widimsky, J. Herget, J. Mkczoch, S. Karger AG (Basel) 1985; **20:** 35.

Complement activation in the adult respiratory distress syndrome following cardiopulmonary bypass. Lew, P.D., Forster, A. *et al. Clinical Respiratory Physiology* 1985; **21:** 231.

Inspiratory muscle function in patients with severe kyphoscoliosis. Lisboa, C., Moreno, R. *et al. American Review of Respiratory Disease* 1985; **132:** 48.

Effects of histamine on bronchial artery blood flow and bronchomotor tone. Long, W.M., Sprung, C.L. *et al. Journal of Applied Physiology* 1985; **59:** 254.

Bronchial hyporesponsiveness. Macklem, P.T. *Chest* 1985; **87:** 158S.

Adenosine-induced bronchoconstriction in asthma—role of parasympathetic stimulation and adrenergic inhibition. Mann, J.S., Cushley, M.J., Holgate, S.T. *American Review of Respiratory Disease* 1985; **132:** 1.

Nitrogen washout and mortality. Menkes, H.A., Beaty, T.H. *et al. American Review of Respiratory*

Disease 1985; **132:** 115.

Effect of the larynx on oscillatory flow in the central airways: a model study. MENON, A.S., WEBER, M.E., CHANG, H.K. *Journal of Applied Physiology* 1985; **59:** 160.

Neural and humoral factors in control of tracheal calibre. MITCHELL, G.S., VIDRUK, E.H. *Journal of Applied Physiology* 1985; **59:** 198.

Pharmacological stimulation of surfactant secretion and surfactant replacement. ROBERTSON, B. *European Journal of Respiratory Diseases* 1985; **67:** 63.

The pulmonary endothelial surface. RYAN, U.S., RYAN, J.W., CRUTCHLEY, D.J. *Federation Proceedings* 1985; **44:** 2603.

Severe pulmonary parenchymal failure—pathophysiological and therapeutic aspects. SUTER, P.M., POLU, J.M. *Clinical Respiration Physiology* 1985; **21:** 219.

Treatment and medication

Fenoterol and ipratropium bromide in respirator treatment of patients with chronic bronchitis. BACKMAN, R., HELLSTROM, R.-E. *Current Therapeutic Research* 1985; **38:** 135.

Periodic breathing triggered by hypoxia in normal awake adults; modification by naloxone. CHADHA, T.S., BIRCH, S., SACKNER, M.A. *Chest* 1985; **88:** 16.

Rehabilitation after severe brain injury—a follow-up study of a behaviour modification approach. EAMES, P., WOOD, R. *Journal of Neurology Neurosurgery and Psychiatry* 1985; **48:** 613.

Treatment of air embolism with hyperbaric oxygen. IRELAND A., POUNDER, D. *et al. British Medical Journal* 1985; **291:** 106.

Experimental evidence that hypoxic pulmonary hypertension can be altered by drugs. KENTERA, D., SUSIC, D., KANJUH, V. *Pulmonary Circulation in Chronic Lung Disease* 1985; **20:** 26.

Anticholinergic drugs in the treatment of airways disease. Review. MANN, J.S., GEORGE, C.F. *British Journal of Diseases of the Chest* 1985; **79:** 209.

Pirbuterol: a preliminary review of its pharmacological properties and therapeutic efficacy in reversible bronchospastic disease. RICHARDS, D.M., BROGDEN, R.N. *Drugs* 1985; **30:** 6.

Thromboxane and prostacyclin in clinical acute respiratory failure. SLOTMAN, G.J., BURCHARD, K.W., GANN, D.S. *Journal of Surgical Research* 1985; **39:** 1.

Methylprednisolone impairs the bactericidal activity of alveolar macrophages. WHITE, J.C., LANSER, M.E. *et al. Journal of Surgical Research* 1985; **39:** 46.

Central nervous system

Physiology

Effects of beta-adrenergic antagonists and agonists on sleep. ADRIEN, J., LANFUMEY, L., DOGOVIC, C. *Sleep: Neurotransmitters and Neuromodulators.* Raven Press (New York) 1985; p. 93.

Dopamine agonists and sleep in man. CIANCHETTI, C. *Sleep: Neurotransmitters and Neuromodulators.* Raven Press (New York) 1985; p. 121.

Spinal pathways mediating respiratory influences on sympathetic nerves. CONNELLY, C.A., WURSTER, R.D. *American Journal of Physiology* 1985; **249:** R91.

Involvement of noradrenaline in wakefulness and paradoxical sleep. GAILLARD, J.M. *Sleep: Neurotransmitters and Neuromodulators.* Raven Press (New York) 1985; p. 57.

Increased digitalis-like activity in human cerebrospinal fluid after expansion of the extracellular fluid volume. HALPERIN, J.A., MARTIN, A.M., SALVADOR, M. *Life Sciences* 1985; **37:** 561.

Paradoxical sleep and chemically identified neurones of the reticular formation. JONES, B.E. *Sleep: Neurotransmitters and Neuromodulators.* Raven Press (New York) 1985; p. 43.

Contribution of the Na^+-K^+ pump to membrane potential in familial periodic paralysis. MARTIN, A.R., LEVINSON, S.R. *Muscle and Nerve* 1985; **8:** 359.

Neurons responsible for paradoxical sleep. SAKAI, K. *Sleep: Neurotransmitters and Neuromodulators.* Raven Press (New York) 1985; p. 29.

Treatment and medication

Prognostic significance of hyperglycaemia in acute stroke. CANDELISE, L., LANDI, G. *et al. Archives of Neurology* 1985; **42:** 661.

Current concepts: neuroleptic malignant syndrome. GUZE, B.H., BAXTER, L.R. *New England Journal of Medicine* 1985; **313:** 163.

Anticonvulsant drug mechanisms of action. MACDONALD, R.L., MCLEAD, M.J., SKERRIT, J.H. *Federation Proceedings* 1985; **44:** 2634.

Effect of mannitol on cerebral blood flow and cerebral perfusion pressure in human head injury. MENDELOW, A.D., TEASDALE, G.M. *et al. Journal of Neurosurgery* 1985; **63:** 43.

Amelioration of hypoxemia by neuromuscular blockade following brain injury. MILLIS, R.M., WOOD, D.H. TROUTH, C.O. *Life Sciences* 1985; **37:** 739.

Continuous intrathecal baclofen for severe spasticity. PENN, R.D., KROIN, J.S. *Lancet* 1985; **2:** 125.

Endocrine and metabolic

Physiology

Natural history of primary myxedema. BASTENIE, P.A., BONNYNS, M., VANHAELST, L. *American Journal of Medicine* 1985; **79:** 91.

Vasopressin—the control of its release and cardiovascular actions. BROOKS, D.P., SHARE, L., CROFTON, J.T. *Vasopressin*. Raven Press (New York) Ed. R.W. Schrier 1985: p. 69.

Hypothalamo-pituitary responses to trauma. Buckingham, J.C. *British Medical Bulletin* 1985; **41:** 203.

Concept of natriuretic hormone. De Wardener, H.E., Clarkson, E.M. *Physiological Reviews* 1985; **65:** 658.

Evidence against role of antidiuretic hormone in support of blood pressure during dehydration. Fejes-Toth, G., Naray-Fejes-Toth, A. *et al. American Journal of Physiology* 1985; **249:** H42.

Serum hormones during prolonged training of neuromuscular performance. Hakkinen, K., Pakarinen, A. *et al. European Journal of Applied Physiology* 1985; **53:** 287.

Interaction of insulin with the renal proximal tubular cell. Hammerman, M.R. *American Journal of Physiology* 1985; **249:** F1.

Overestimation of renal function in glucocorticosteroid treated patients. Horber, F.F., Scheldegger, J., Frey, F.J. *European Journal of Clinical Pharmacology* 1985; **28:** 537.

Opiates and vasopressin secretion. Kamoi, K., Robertson, G.L. *Vasopressin*. Raven Press (New York) Ed. R.W. Schrier 1985: p. 259.

Fluid and electrolyte disturbances after trauma: the role of adrenocortical and pituitary hormones. Le Quesne, L.P., Cochrane, J.P., Fieldman, N. *British Medical Bulletin* 1985; **41:** 212.

The metabolic response of the kidney to acute sodium lactate alkalosis. Lemieux, G., Junco, E. *et al. Canadian Journal of Physiology and Pharmacology* 1985; **63:** 687.

Physiological and pharmacological studies of the adrenal medulla by measurement of the plasma catecholamine levels. Lhoste, F. *Journal de Pharmacologie* 1985; **16:** 139 (Suppl 1).

Effects of arginine vasopressin on regional circulations. Liard, J.F. *Vasopressin*. Raven Press (New York) Ed. R.W. Schrier 1985; p. 59.

Evidence that a benzodiazepine receptor mechanism regulates the secretion of pituitary beta-endorphine in rats. Maiewski, S.F., Larscheid, P. *et al. Endocrinology* 1985; **117:** 474.

Sequential changes in circulating total protein and albumin masses after abdominal vascular surgery. Nielsen, O.M. *Annals of Surgery* 1985; **202:** 231.

Central venous pressure and plasma arginine vasopressin during water immersion in man. Norsk, P., Bondepetersen, F., Warberg, J. *European Journal of Applied Physiology* 1985; **54:** 71.

Metabolic utilization and renal handling of D-lactate in men. Oh, M.S., Uribarri, J. *et al. Metabolism. Clinical and Experimental* 1985; **34:** 621.

Serum osmolality in acute intoxication: a prospective clinical study. Pappas, A.A., Gadsen, R.H., Taylor, E.H. *American Journal of Clinical Pathology* 1985; **84:** 74.

Human fibronectin metabolism. Pussell, B.A., Peake, P.W. *et al. Journal of Clinical Investigation* 1985; **76:** 143.

Vasopressin facilitates baroreceptor inhibition of sympathetic vasomotor activity by more than one mechanism. Schmid, P.G., Guo, G.B. *et al. Vasopressin*. Raven Press (New York) Ed. R.W. Schrier 1985; p. 11.

Kidney function during arterial chemoreceptor stimulation. I. Schmidt, M., Ledderhos, C., Honig, A. *Biomedica Biochimica Acta* 1985; **44:** 695.

Kidney function during arterial chemoreceptor stimulation. II. Schmidt, M., Wedler, B. *et al. Biomedica Biochimica Acta* 1985; **44:** 711.

Reversible diabetic nerve dysfunction: structural correlates to electrophysiological abnormalities. Sima, A.A.F., Brismar, T. *Annals of Neurology* 1985; **18:** 21.

Effect of insulin on the distribution and disposition of glucose in man. Smith, J.D., Cobelli, C. *et al. Journal of Clinical Investigation* 1985; **76:** 357.

Adrenal function in asthmatics treated with high-dose budesonide. Stiksa, G., Nemcek, K., Glennow, C. *Respiration* 1985; **48:** 91.

Competitive antagonists of bradykinin. Vavrek, R.J., Stewart, J.M. *Peptides* 1985; **6:** 161.

Insulin action on membrane potential and glucose uptake: effects of high potassium. Zierler, K., Rogus, E.M. *et al. American Journal of Physiology* 1985; **249:** E17.

Treatment and medication

Clinical pharmacology of loop diuretics: a comparative study. Ansuini, R., Pulido, M. *et al. International Journal of Clinical Pharmacology Research* 1985; **5:** 113.

Diuretics hypokalemia and ventricular ectopy. Atwood, J.E., Gardin, J.M. *Archives of Internal Medicine* 1985; **145:** 1185.

Glucose counterregulation, hypoglycemia, and intensive insulin therapy in diabetes mellitus. Bryer, P.E., Gerich, J.E. *New England Journal of Medicine* 1985; **313:** 232.

Pain

Physiology

The relationship of peripheral trauma and pain to dystonia. Schott, G.D. *Journal of Neurology Neurosurgery and Psychiatry* 1985; **48:** 698.

Treatment and medication

Self-administered nalbuphine, morphine and pethidine. Comparison, by intravenous route, following cholecystectomy. Bahar, M., Rosen, M., Vickers, M.D. *Anaesthesia* 1985; **40:** 529.

Postoperative pain and pulmonary complications: comparison of three analgesic regimens. Cushieri, R.J., Morran, C.G. *et al. British Journal of Surgery* 1985; **72**: 25.

Relief of pain by infusion of morphine after operation: does tolerance develop? Marshall, H., Porteous, C. *et al. British Medical Journal* 1985; **291**: 19.

The assessment of pain and plasma beta-endorphin immunoactivity in burned children. Szyfelbein, Osgood, P.F., Carr, D.B. *Pain* 1985; **22**: 173.

Stop Press

Courses in Anaesthesia

FFARCS Part 1

Leicester Royal Infirmary, Leicester, LE1 5WW.	3–7 February 1986 1 week whole time block course	NO FEE	The Secretary, Department of Anaesthesia, Leicester Royal Infirmary, Leicester, LE1 5WW *Tel.* 0533 541414 *Ext.* 474

FFARCS Part 2

Leicester Royal Infirmary, Leicester, LE1 5WW.	11 October 1985– 11 April 1986 Friday afternoons	NO FEE	The Secretary, Department of Anaesthesia, Leicester Royal Infirmary Leicester, LE1 5WW *Tel.* 0533 541414 *Ext.* 474.

FFARCS Part 3 (Final)

Leicester Royal Infirmary, Leicester, LE1 5WW.	5 September– 17 October 1986 Friday afternoons	NO FEE	The Secretary, Department of Anaesthesia, Leicester Royal Infirmary, Leicester, LE1 5WW *Tel.* 0533 541414 *Ext.* 474.

Other courses

REVISION COURSE Leicester Royal Infirmary, Leicester, LE1 5WW.	2 May–27 June 1986, Friday afternoons. 21–25 April 1986 1 week whole time block course	FEE ON APPLICATION	The Secretary, Department of Anaesthesia, Leicester Royal Infirmary, Leicester, LE1 5WW *Tel.* 0533 541414 *Ext.* 474.

Notice to contributors to *Anaesthesia*

Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Articles accepted become copyright of *Anaesthesia.*

Contributors are requested to submit two copies of manuscripts. They are also advised to retain a third copy as the Editors cannot accept responsibility for the loss of manuscripts in the post. The covering letter should be signed personally by all the authors and careful consideration should be given to the decision to include more than five authors. Articles should be forwarded to:

Dr J. N. Lunn, Editor of ***Anaesthesia****, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.*

PREPARATION OF MANUSCRIPTS

Articles for *Anaesthesia* should be prepared in accordance with *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5) except that the titles of journals in the reference section should be given in full (see below). A reprint of these requirements of which this notice is a summary, can be obtained from the *British Medical Journal* price 50 pence (U.K.).

Type manuscripts on white bond paper, 20.3 × 26.7 cm or 21.6 × 27.9 cm (8 × 10¼ in. or 8½ × 11 in.) or ISO A4 (212 × 297 mm) with margins of at least 2.5 cm (1 in.). Use double, and preferably triple, spacing throughout, including the references. Please do not use a dot matrix printer, particularly one with poor quality descenders or ascenders. Unseparated, fan-folded manuscripts may be returned to the author.

The manuscript should consist of the following sections in this order each beginning on a new page: *title page, summary* and *key words, text, acknowledgments, references, individual tables*, and *legends for figures.*

Number pages consecutively, beginning with the title page. Type the page number in the upper right-hand corner of each page.

THE TITLE PAGE

The name of the author and the address to which proofs and other correspondence is to be addressed should appear in the top left-hand corner of the sheet.

The main title should be restricted to five words if this is possible. It should be typed in capitals across the centre of the title page.

A subsidiary title of not more than 12 words may be supplied if this is considered to be necessary. This should be typed in lower case immediately beneath the main title.

The names of the authors should be typed IN CAPITALS across the title page immediately beneath the titles without degrees or designations. Initials should precede the surname. One forename may be given in full according to the author's preference. If there is more than one author the word 'AND' should be placed before the name of the last author.

A line should be typed across the title page below the author(s) name(s) in capitals.

The author(s) name(s) degrees and designations should be typed in lower case below the line. Initials and or forename should precede the name of each author and his degrees, without full stops between letters, and appointment (e.g. Consultant, Registrar, etc.) should follow it.

A full postal institutional address should follow the names, degrees and appointments. Correspondence will normally be addressed to the first author but, if it is desired to direct correspondence other than to the first author, or if different authors belong to different institutions or departments, a separate sentence should be added: this should start on a new line and begin 'Correspondence should be addressed to ...' and a full postal address should follow.

SUMMARY AND KEY WORDS

Start a new sheet

The second page should carry a summary of not more than 150 words. The summary should state the purpose of the study or investigation, basic procedures, main findings and their statistical significance, and the principal conclusions.

Do not use abbreviations except for units of measurement (e.g. mg, cm, etc.).

Key (indexing) words. Below the abstract, provide and identify as such, three to 10 key words or short phrases that will assist indexers. Use terms from the Medical Subject Headings list from *Index Medicus.* The Editor may modify these at proof stage to conform with agreed practice of certain other anaesthetic journals in the English language.

COPYRIGHT OFFPRINTS

Authors submitting a manuscript do so on the understanding that if it is accepted for publication, exclusive copyright in the paper shall be assigned to the Association. In consideration for the assignment of copyright, the Publisher will supply 25 offprints of each paper. Further offprints may be ordered at extra cost; the copyright assignment form and the offprint order form will be sent with the proofs. The Association will not put any limitation on the personal freedom of the author to use material contained in the paper in other works.

(continued overleaf)

THE TEXT

Start a new sheet

The text of observational and experimental articles, case reports, etc. is usually divided into sections with the headings *Introduction, Methods, Results* and *Discussion*. Long articles will need subheadings within some sections to clarify their content.

Letters for the correspondence pages should be double spaced and prepared in accordance with the format in a recent copy of *Anaesthesia*.

Headings: three steps of heading may be used in typescripts:

(i) CAPITALS across the centre of the page.
(ii) Underlined words
These should be typed at the left hand side of the page above the paragraph which they precede.
(iii) Underlined words at the beginning of a paragraph. These may either be followed by a full stop or form part of the first sentence of the paragraph.

ACKNOWLEDGMENTS

Start a new sheet

Acknowledge those who have made substantive contributions to the study or the preparation of the manuscript. Authors are responsible for obtaining written permission for publication of reproduced figures and tables from authors and publishers and from everyone acknowledged by name because of copyright conventions and because readers may infer their endorsement of the data and conclusions.

REFERENCES

Start a new sheet

Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by arabic numerals. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. Use double or treble space typing.

Use the form of reference adopted by the U.S. National Library of Medicine and used in *Index Medicus*. Use the style of the examples cited at the end of this section.

The titles of journals should be given in full.

Avoid using abstracts as references except those published in a recognised journal. 'Unpublished observations' and 'personal communications' may not be used as references, although references to written, not verbal, communications may be inserted (in parentheses) in the text. Include among the references manuscripts accepted but not yet published; designate the journal followed by (*in press*) in parentheses. Information from manuscript submitted but not yet accepted should be cited in the text as (unpublished observations) in parentheses.

The references must be verified by the author(s) against the original documents.

Examples of correct form of references
Note: first and last pages in all references.

JOURNAL

Standard journal article—(List all authors)

SOTER NA, WASSERMAN SI, AUSTEN KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294:** 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

OSLER AG. *Complement: mechanisms and functions.* New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. AMA drug evaluations. 3rd ed. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

RHODES AJ, VAN ROOVEN CE, *comps. Textbook of virology: for students and practitioners of medicine and other health sciences.* 5th ed. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

WEINSTEIN L, SWARTZ MN Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease.* Philadelphia: WB Saunders, 1974: 457–72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, Md: National Center for Health Statistics, 1972. (*Vital and health statistics. Series* **10:** Data drom the National Health Survey, No. 69) [DHEW publication No. (HSM) 72-1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

ROUECHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

TABLES

Do not include tables in the text. Start a new sheet for each table and space the material adequately. The author(s) name(s) should appear in the top right-hand corner.

Indicate the approximate position of each table in relation to the subject matter of the text in the right-hand margin of the appropriate page on the manuscript. Do not submit tables as photographs. Number tables consecutively with arabic numerals. Supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes. Explain in footnotes all non-standard abbreviations that are used in each table. For footnotes, use the following symbols in this sequence: *, †, ‡, §, ||, ¶, **, ††, etc. Identify statistical measures of variations such as SD and SEM. *Legends for tables* should appear on the face of the table.

Cite each table in the text in consecutive order and mark the approximate position of the table in the right-hand margin of the text.

FIGURES

Each figure should be separate. Do not include figures in the text but collect together in an envelope or folder.

Indicate the approximate position of each figure in relation to the subject matter of the text in the right-hand margin of the appropriate page of the manuscript. Drawings, charts and diagrams should be submitted in black indian ink on a smooth white card and should be about twice the size of that desired in the published version with no lettering. Full plate, glossy black and white photographs will be accepted if they are sufficiently clear. All letters and numerals required on the face of figures must be clearly typed or written on tracing paper firmly attached with self-adhesive tape to the back of the figure and folded over from the front as a cover. They will then be printed in the style of *Anaesthesia* in the exact location indicated. Identify each figure by its sequential number in pencil on the reverse of the illustration and include the title of the paper and the authors' names. Mark the top of the illustration on the reverse by an arrow and the word 'Top'.

All sources of identification of patients must be removed.

LEGENDS FOR FIGURES

Start a new sheet

Type legends for illustrations double spaced with arabic numerals corresponding to the illustrations. When symbols, arrows, numbers or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

CONVENTIONS AND ABBREVIATIONS

Statistics and measurements should be given in figures except that numerals one to nine should be in words if not followed by a measurement symbol (e.g. 'two patients' but '2.0 mg'). The *Système International* (SI) will usually be used except that vascular pressures will be recorded in mmHg and cmH_2O. Imperial measurements will not be used except in an historic context. The 24 hour clock will be used.

Contributors are advised to study the SI *Conversion Tables* provided in the January 1978 issue of *Anaesthesia*, *Units, Symbols and Abbreviations* (*A Guide for Biological and Medical Editors and Authors*) published by the Royal Society of Medicine, London W1M 8AE, and *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5).

LETTERS FOR PUBLICATION

Should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University of Wales Hospital, Heath Park, Cardiff CF4 4XW, UK.

Letters should be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters above. The degrees and diplomas of each author must be given in a covering letter which must be signed personally by all the authors.

Correspondence presented in any other style or format may be the subject to considerable delay and may be returned to the author for revision.

The editors regret that failure to comply with the above requirements may result in a delay in publication of accepted papers.

REVIEW JOURNALS

This journal is covered by *Current Contents*, *ASCA* and the *Science Citation Index*.

Contents: Anaesthesia, vol. 41, no. 2, February 1986

EDITORIAL

A matter of vigilance 129
R. Green

ORIGINAL ARTICLES

Nuclear magnetic resonance. Its implications for the anaesthetist
C. Nixon, N.P. Hirsch, I.E.C. Ormerod and G. Johnson 131
In vitro buffering capacity of Alka Seltzer Effervescent. A comparison with magnesium trisilicate mixture B.P. and sodium citrate 0.3 M
G.C. Murrell and M. Rosen 138
Continuous infusion epidural analgesia in obstetrics. A comparison of 0.08% and 0.25% bupivacaine
A. Ewen, D.D. McLeod, D.M. MacLeod, Alison Campbell and M.E. Tunstall 143
Bacterial contamination of compressed air for medical use
P. Bjerring and B. Øberg 148
Time course of action of combinations of vecuronium and pancuronium
S.K. Pandit, C.J. Ferres, F.M. Gibson and R. K. Mirakhur 151
Plasma bupivacaine concentrations following psoas compartment block
J.A. Odoom, W.W.A. Zuurmond, I.L. Sih, J. Bovill, G. Österlöf and H.V. Oosting 155
Pretreatment with opioids. The effect on thiopentone induction requirements and on the onset of action of midazolam
J.W. Dundee, N.J. Halliday, T.J. McMurray and K.W. Harper 159
The haemodynamic effects of bronchoscopy. Effect of pretreatment with fentanyl and alfentanil
Katheryn J. Wark, J. Lyons and R. O. Feneck 162
Assisted ventilation and the Servo ventilator in infants. An assessment of three systems used for CPAP/IMV
R.M. Bingham, D.J. Hatch and P.J. Helms 168
Monitoring EEG frequency and amplitude during cardiac surgery
A. Murray, A.P. Glaria and D.T. Pearson 173
Anaphylactoid reaction complicating neonatal anaesthesia
E.M.M. Pollock, A.D. MacLeod and L.R. McNicol 178

CASE REPORT

All that wheezes is not asthma
A.R. Lloyd-Thomas and G.H. Bush 181
Amiodarone, phaeochromocytoma and cardiomyopathy
G. Solares, F. Ramos, R. Martín-Durán, J.M. San-José and M. Buitrago 186
Anaesthesia for surgical occlusion of the basilar artery. A technique involving intra-operative awakening to allow neurological assessment
C.S. Child, M.P.D. Heining, I. Calder and H.A. Crockard 191

APPARATUS

A new device for the inflation of the antigravity suit
P.M. Brodrick 195
An evaluation of the Datex Normac anaesthetic agent monitor
A.D. Colquhoun, W.M. Gray and A.J. Asbury 198

FORUM

Local complications following intravenous benzodiazepines in the dorsum of the hand. A comparison between midazolam and Diazemuls in sedation for dentistry
J.J. Margary, N.L. Rosenbaum, M. Partridge, S. Shankar 205

CORRESPONDENCE 208

BOOK REVIEWS 227

AUDIOVISUAL REVIEWS 229

INDEX OF COMPUTER PROGRAMS 231

ANAESTHETIC LITERATURE 232

STOP PRESS 240

Printed in Great Britain by Fletcher & Son Ltd, Norwich

Acc.
25.9.87

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain & Ireland

Volume 41 Number 3 March 1986

Published for
The Association of Anaesthetists of Great Britain and Ireland by

Academic Press
London Orlando San Diego New York Toronto
Montreal Sydney Tokyo

ISSN 0003-2409

Ventilation takes a step forward.

Working closely with the anaesthesia profession worldwide for more than 60 years, Ohmeda has developed some of the world's finest medical equipment.

Our joint efforts have produced a formula that has worked effectively, and the results are evident in our latest development: the OAV 7700 anaesthesia ventilator.

One of the most advanced anaesthesia ventilators available to date, the OAV 7700 offers the accuracy of electronic control combined with the reliability of pneumatically operated lung ventilation.

A highly flexible unit, the OAV 7700 can be used in either open or closed circuit applications. This unit also offers fully integrated alarms and a clear and immediate display of all patient breathing parameters.

Used in conjunction with the Boyle 2000 or International 2 anaesthesia machines, the OAV 7700 becomes part of a highly reliable, easy to use, cost effective anaesthesia system. One designed with your help . . . to meet your needs.

Specify Ohmeda – We won't let you down.

SPECIALIST CARE FOR SPECIALIST PEOPLE.

Ohmeda

Ohmeda
Elizabeth Way Harlow Essex CM19 5AB England
0279 29692 Telex 81497

BOC Health Care

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

Editorial Board
Editor J. N. LUNN
Assistant Editors M. MORGAN, C. E. BLOGG, R. GREENBAUM, R. M. JONES
Chairman P. J. HELLIWELL
Advisory Editors R. S. ATKINSON, T. B. BOULTON
Members C. F. SCURR, P. J. F. BASKETT, D. J. HATCH and a representative of the Junior Anaesthetists Group
Ex officio
The President of the Association T. B. BOULTON
The Honorary Treasurer of the Association M. M. BURROWS
The Honorary Secretary of the Association M.T. INMAN
The Assistant Honorary Secretary of the Association P. MORRIS

Editor Emeritus C. LANGTON HEWER

Sub-editors of special sections
L. KAUFMAN Anaesthetic literature
A. PADFIELD National and local events
G. D. PARBROOK Audiovisual reviews
M. J. HARRISON Computer programs
JACQUELINE WELCH, DIANE WINTERBURN Reference librarians
D. V. BATEMAN Honorary proof reader

Address for literary contributions Dr J. N. Lunn, The Editor, *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK [telephone Cardiff (0222) 763601; Ansafone available].

Neither the Editor nor the Association of Anaesthetists of Great Britain and Ireland is in any way responsible for the statements made or the views expressed by contributors.
Investigations performed on man must conform to appropriate ethical standards including voluntary consent and acceptance by an ethical committee.

Published monthly (January–December) at 24–28 Oval Road, London NW1 7DX, England by Academic Press Inc. (London) Limited for the Association of Anaesthetists of Great Britain and Ireland, Rooms 475–478, Tavistock House South, Tavistock Square, London WC1H 9LG. As from December 2nd 1985, 9 Bedford Square, London WC1B 3RA.
1986, Volume 41, 12 issues. Inland £80.00 inclusive of postage and packing; abroad, $189.00 inclusive of postage and packing
Subscription orders should be sent to Academic Press Inc. (London) Limited, High Street, Foots Cray, Sidcup, Kent DA14 5HP (Tel. 01-300-0155). Send notices of change of address to the office of the Publishers at least 6–8 weeks in advance. Please include both old and new addresses.
Application to pay at second class postage rates pending at Jamaica, New York 11431, U S A
Air freight and mailing in the U S A by Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, U S A
© 1986 The Association of Anaesthetists of Great Britain and Ireland. The appearance of the code at the bottom of the first page of a paper in this journal indicates the copyright owner's consent that copies of the paper may be made for personal or internal use, or for the personal or internal use of specific clients in the U S A. This consent is given on the condition, within the U S A., that the copier pay the stated per-copy fee through the Copyright Clearance Center Inc., 27 Congress Street, Salem, MA 01970, U S A for copying beyond that permitted by Sections 107 or 108 of the U S Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, for resale or for copying or distributing copies outside the U S A.

ISSN 0003-2409

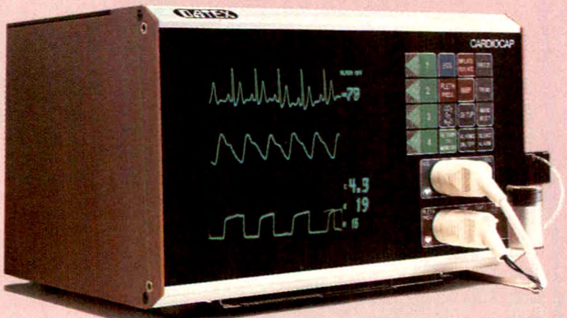
Two breath taking advan
from Vickers Medical

Vickers Medical maintains its position at the forefront of patient monitoring systems with the launch of two outstanding new anaesthetic monitors – Cardiocap and Multicap. Both units incorporate the most sophisticated innovations in sensor and microcomputer technology. They are compact, cost-effective and versatile, and greatly enhance the efficiency of the operating theatre and recovery room.

MULTICAP

This is the newest addition to the Vickers Medical range of respiratory gas monitors. Multicap is simple to operate and economical to run. Its sampling system is controlled by microprocessors which guarantee reliable operation, while its six displays give you simultaneous, at-a-glance data on essential physiological functions.

- **Miniature sensors – unique to Vickers Medical – have ultra-fast response time which allows "breath-by-breath" measurement of CO_2, N_2O and O_2**
- **Easy use of communications capabilities guaranteed by complete software control**
- **Audio and visual alarms on major parameters monitored**
- **Sensor requires no servicing**



CARDIOCAP

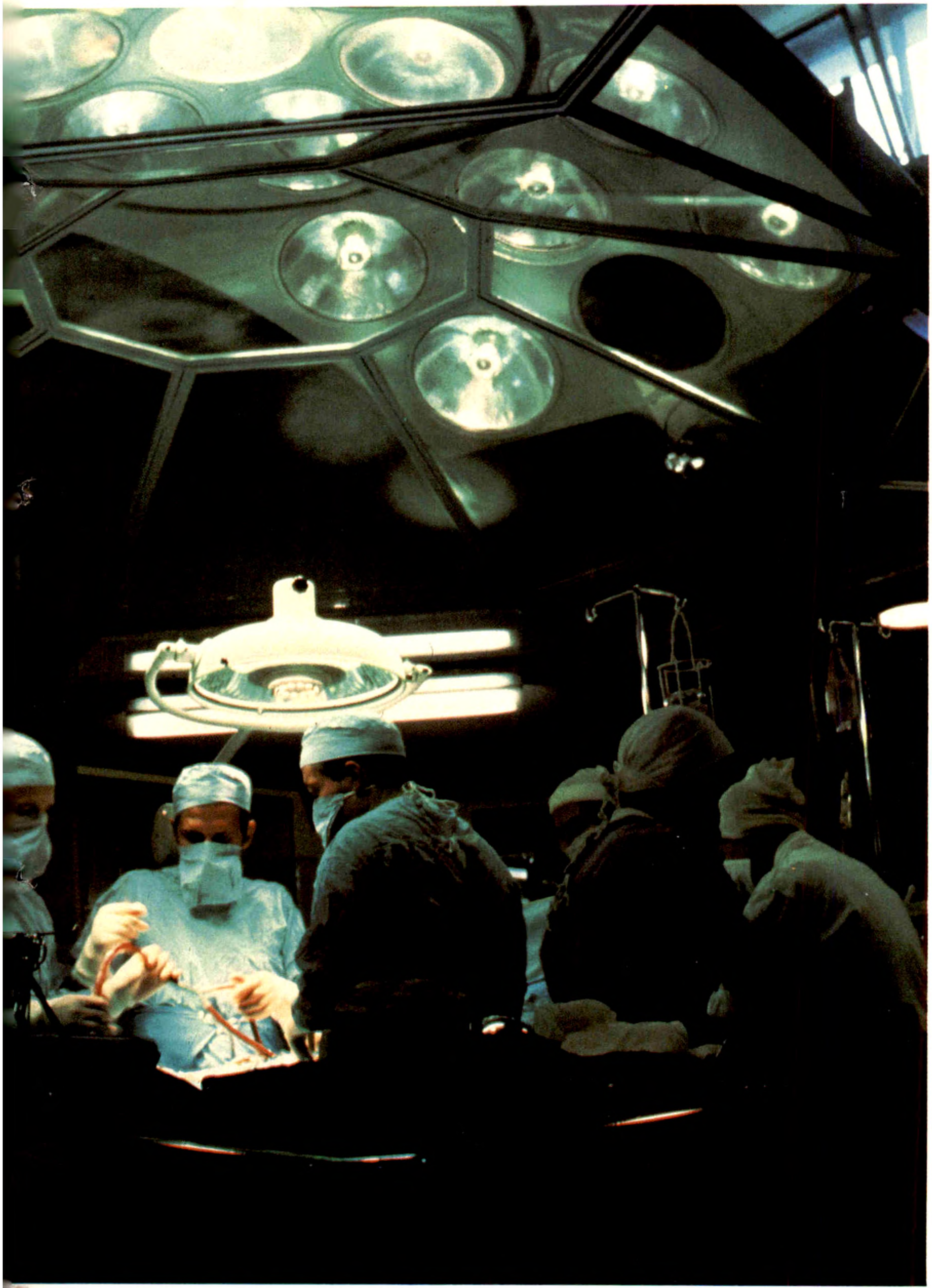
This integrated non-invasive monitor is unique in that, as a single unit, it displays all the vital respiratory and circulatory information you need at a glance.

- **ECG** ■ **Digital heart rate**
- **Breath-by-breath CO_2, O_2 and N_2O**
- **Integral, non-invasive blood pressure wave-form and digital value**
- **Plethysmographic Pulse/Invasive Blood Pressure Wave-Form**
- **Two temperature channels**
- **Complete communication capability**

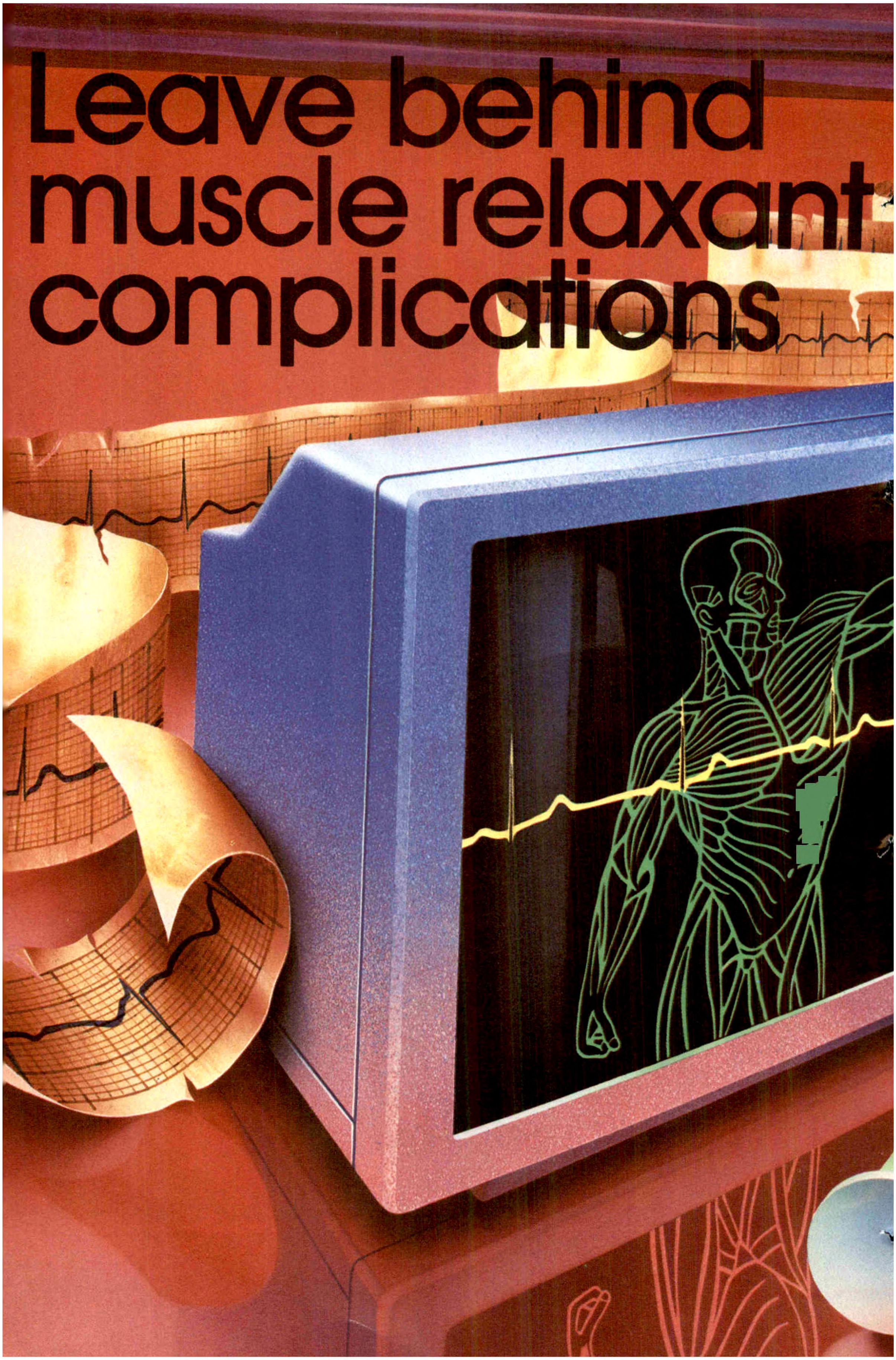
For further information, contact
Nick Tyrrell, Product Manager,
Vickers Medical, Priestley Road,
Basingstoke, Hampshire,
England RG24 9NR.
Telephone 0256-29141.
Telex 858697. FAX 0256460802

Vickers
Medical

Cardiocap and Multicap are registered trademarks of Instrumentarium Corporation and are manufactured in Finland by Datex.



Anaesthesia monitoring at its most advanced


Leave behind
muscle relaxant
complications

Muscle relaxation, pure and simple

NORCURON®

vecuronium bromide

Highly specific

Muscle relaxants are known to cause cardiovascular side effects when their action is not specific for the neuromuscular junction.

NORCURON

"...is the most specific neuromuscular blocking agent that has ever been synthesized. It is the drug which has by far the fewest side effects of any neuromuscular blocker. As a result, it has the highest therapeutic ratio".[1]

NORCURON

"Because it is so 'pure', because it is so free from side effects, it can be given in high doses. It can be given at 6, 8, 10 or 15 times the ED_{90} dose, if the clinician so wishes".[1]

Histamine release unlikely

Some muscle relaxants cause histamine release. This may give rise to such side effects as hypotension and bronchospasm.

NORCURON

"...at 3.5 times the ED_{95} does not alter serum histamine levels".[2]

NORCURON

Muscle relaxation, pure and simple.

ORGANON TEKNIKA

Organon Teknika Limited

Cambridge Science Park, Milton Road,
Cambridge CB4 4BH

1. Feldman SA; Clinical Experiences with Norcuron, Excerpta Medica (1983) 199-200
2. Basta SA; Clinical Experiences with Norcuron, Excerpta Medica (1983) 183-184

NORCURON ampoules of 4mg vecuronium bromide with 1ml ampoule water for injection. **Uses:** non-depolarising neuromuscular blocking agent of short to medium duration. **Dosage:** intravenous initial 0.08 to 0.10mg/kg incremental 0.03 to 0.05mg/kg. **Contra-indications:** none known. Since there is no experience with the use of Norcuron in pregnant women, it cannot be recommended during pregnancy. Clinical studies show that Norcuron can be used in childbirth by Caesarian section without effect on the newly born child. **Precautions and warnings:** in renal insufficiency a slight prolongation of neuromuscular block can be expected. Use very small doses, and extreme caution in myasthenia gravis or myasthenic syndrome unless prolonged post-operative respiratory assistance is intended. Dose carefully in myopathy, severe obesity, electrolyte disturbances, altered pH and after poliomyelitis or dehydration. Neuromuscular blockade can be reversed with adequate doses of neostigmine together with atropine. **Interactions:** it is dangerous to give depolarising drugs (e.g. suxamethonium chloride) following a non-depolarising drug (e.g. Norcuron). Alkylating drugs (nitrogen mustards) may be a hazard in anaesthesia involving muscle relaxants. Anaesthetics, other drugs and the condition of the patient, may affect the magnitude and or duration of action of NORCURON – see Data Sheet. **Side-effects:** none during clinical testing. **Overdosage:** use standard reversal agents. e.g. neostigmine or pyridostigmine. **Packs:** 50 ampoules 4mg NORCURON, 50 ampoules 1ml solvent. **PL:** 3524/0009.

THE BRISTOL CRAMMER

Final F.F.A. Exam
Intensive Course

28th April–2nd May 1986

This five day Course will include tutorials on current topics, practical subjects viz ECGs, X-rays, Equipment and examination of clinical cases. Sessions will be conducted by national and local experts and will include mock examinations and performance analyses.

Course Fee £100 *Closing date: 18th April*

Further details from: **Anaesthetic Secretary, Department of Anaesthetics, Frenchay Hospital, Bristol. Telephone (0272) 565656 Extension 2640/2641.**

Hespan

Hetastarch 6%

In place of
plasma in hypovolaemia

Further information is available on request
American Hospital Supply (U.K.) Ltd.
Wallingford Road, Compton, Nr. Newbury,
Berkshire RG16 0QW.

WE'VE GIVEN YOU PRECISELY WHAT YOU WANTED

MORE DILUTE HYPNOVEL

When we asked how Hypnovel could be improved, many users asked for a more dilute presentation, so that finer control of dosage, and therefore sedation, could be achieved. So the 2ml presentation was joined by an ampoule containing the same 10mg of midazolam, but in 5ml of solution. The extra 3ml of diluent makes it simpler to obtain the full benefits of Hypnovel. Proven benefits of Hypnovel include fast onset and rate of recovery, excellent amnesia and minimal venous complications.[1]

THE HYPNOVEL 10mg/5ml AMPOULE

midazolam

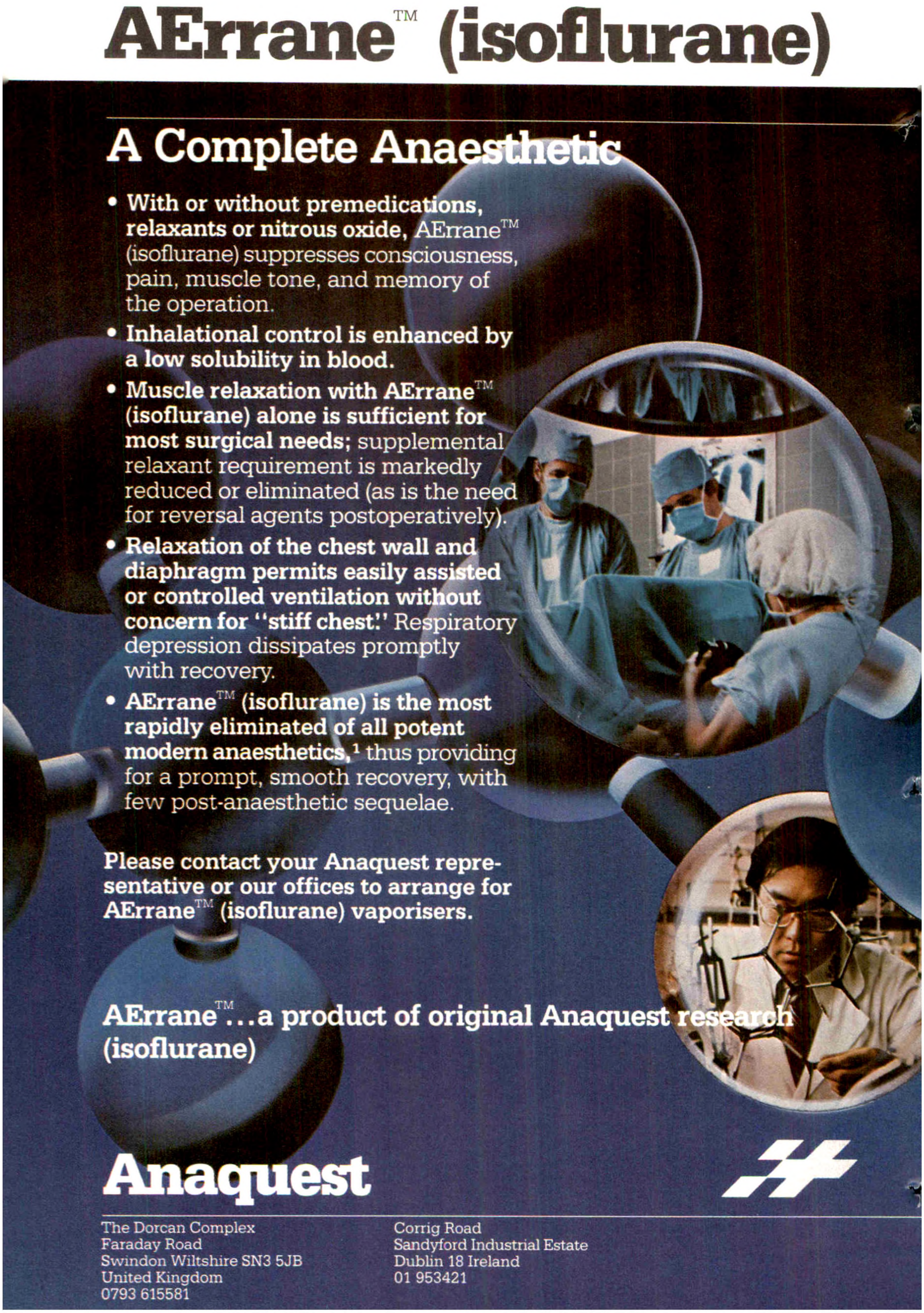
FOR MORE PRECISE CONTROL OF I.V. SEDATION

Prescribing Information

Indications Intravenous sedative cover. Alternative intravenous agent for induction of anaesthesia in high-risk patients. Intramuscular premedication. **Dosage and Administration** *Intravenous sedation* Usual total dose 2.5mg to 7.5mg (approx. 0.07mg/kg body-weight). *Intravenous induction of anaesthesia* Unpremedicated patients: 0.3mg/kg body-weight or more. Premedicated patients: 0.2mg/kg body-weight may be adequate. *Intramuscular premedication* (10mg/2ml ampoule only) Usual dose about 5mg (approx. 0.07-0.1mg/kg body-weight). Elderly patients are more sensitive to the effects of Hypnovel and lower doses should be used. Children over the age of seven years may receive Hypnovel for induction of anaesthesia in a dose of 0.15mg/kg body-weight. **Contra-indications** Benzodiazepine sensitivity; acute pulmonary insufficiency; respiratory depression. **Precautions** Use during pregnancy and lactation should be avoided. Patients should not drive or operate machinery for eight hours after administration. Avoid alcohol. Sedative effects of other centrally-acting drugs may be intensified. For the administration of Hypnovel a second person should always be present and facilities for resuscitation should always be available. **Side-effects** Hypnovel is well tolerated and changes in arterial blood pressure, heart rate and respiration are usually slight. The rapid injection of a high dose can induce soft-tissue airway obstruction or apnoea of short duration. Local effects on veins are infrequent. However, pain on injection and thrombophlebitis may occur. **Presentation** Ampoules containing 10mg midazolam base as the hydrochloride in 5ml or 2ml aqueous solution, in packings of 10. **Basic NHS Cost** 76p per 10mg/5ml ampoule. 64p per 10mg/2ml ampoule. **Product Licence Numbers** 0031/0189 (10mg/5ml), 0031/0126 (10mg/2ml). **Product Licence Holder** Roche Products Limited, PO Box 8, Welwyn Garden City, Hertfordshire AL7 3AY. **Reference** 1. Anaesthesia. 1982, **37**, 1002.
Hypnovel is a trade mark.

ROCHE

J391096/286



AErrane™ (isoflurane)

A Complete Anaesthetic

- **With or without premedications, relaxants or nitrous oxide,** AErrane™ (isoflurane) suppresses consciousness, pain, muscle tone, and memory of the operation.
- **Inhalational control is enhanced by a low solubility in blood.**
- **Muscle relaxation with AErrane™ (isoflurane) alone is sufficient for most surgical needs;** supplemental relaxant requirement is markedly reduced or eliminated (as is the need for reversal agents postoperatively).
- **Relaxation of the chest wall and diaphragm permits easily assisted or controlled ventilation without concern for "stiff chest."** Respiratory depression dissipates promptly with recovery.
- **AErrane™ (isoflurane) is the most rapidly eliminated of all potent modern anaesthetics,**[1] thus providing for a prompt, smooth recovery, with few post-anaesthetic sequelae.

Please contact your Anaquest representative or our offices to arrange for AErrane™ (isoflurane) vaporisers.

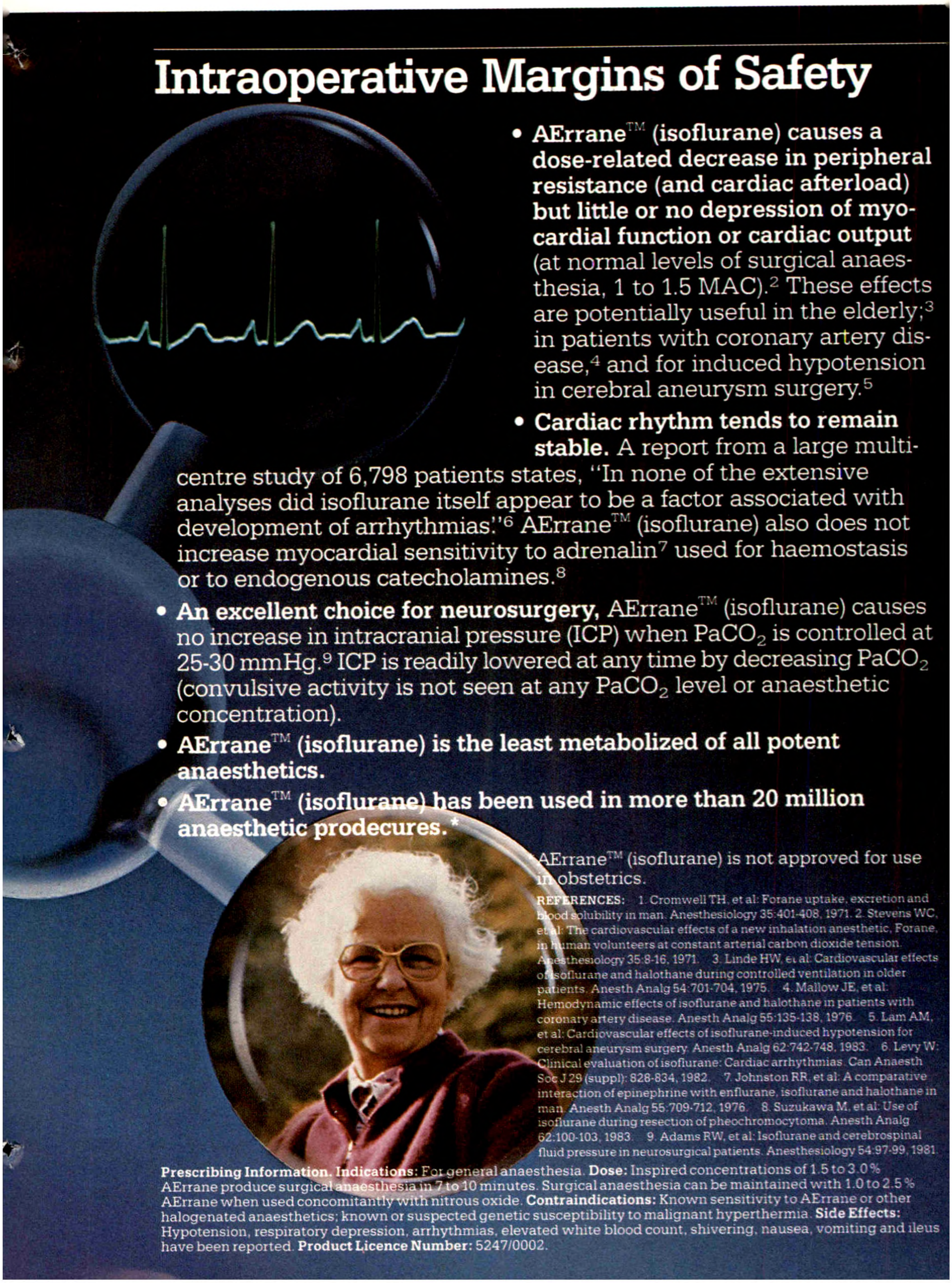
AErrane™...a product of original Anaquest research (isoflurane)

Anaquest

The Dorcan Complex
Faraday Road
Swindon Wiltshire SN3 5JB
United Kingdom
0793 615581

Corrig Road
Sandyford Industrial Estate
Dublin 18 Ireland
01 953421

For the Sum of Your Patient's Anaesthetic Needs



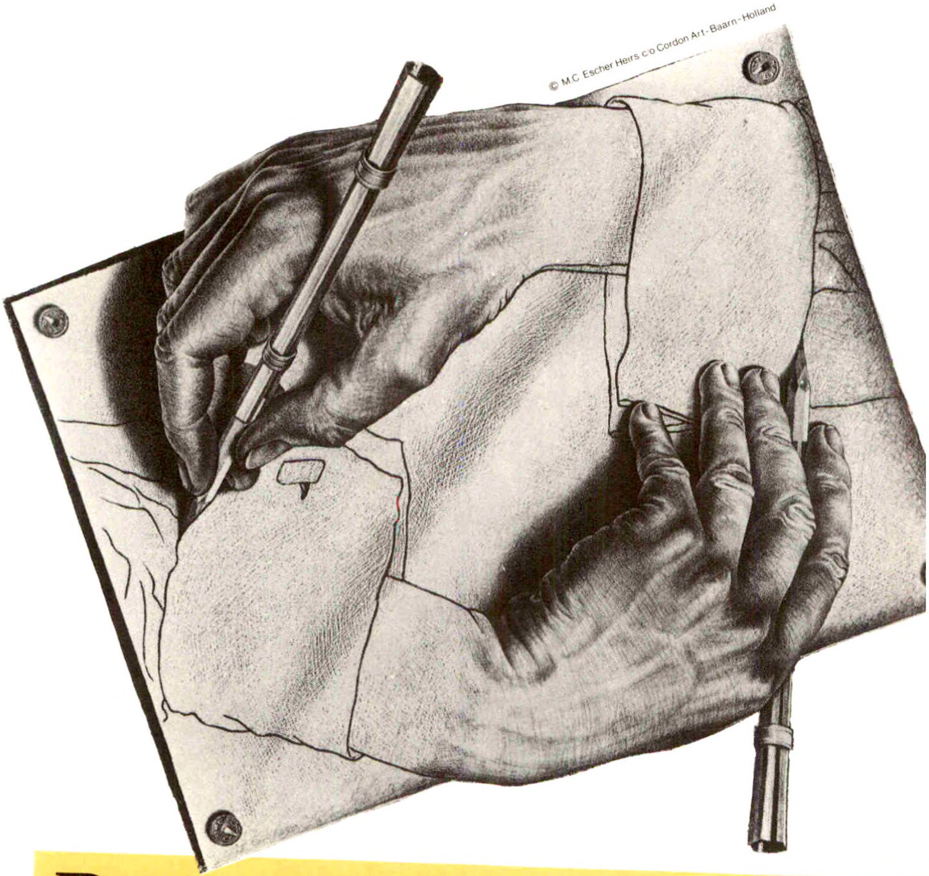
Intraoperative Margins of Safety

- **AErrane™ (isoflurane) causes a dose-related decrease in peripheral resistance (and cardiac afterload) but little or no depression of myocardial function or cardiac output** (at normal levels of surgical anaesthesia, 1 to 1.5 MAC).[2] These effects are potentially useful in the elderly;[3] in patients with coronary artery disease,[4] and for induced hypotension in cerebral aneurysm surgery.[5]
- **Cardiac rhythm tends to remain stable.** A report from a large multicentre study of 6,798 patients states, "In none of the extensive analyses did isoflurane itself appear to be a factor associated with development of arrhythmias."[6] AErrane™ (isoflurane) also does not increase myocardial sensitivity to adrenalin[7] used for haemostasis or to endogenous catecholamines.[8]
- **An excellent choice for neurosurgery,** AErrane™ (isoflurane) causes no increase in intracranial pressure (ICP) when $PaCO_2$ is controlled at 25-30 mmHg.[9] ICP is readily lowered at any time by decreasing $PaCO_2$ (convulsive activity is not seen at any $PaCO_2$ level or anaesthetic concentration).
- **AErrane™ (isoflurane) is the least metabolized of all potent anaesthetics.**
- **AErrane™ (isoflurane) has been used in more than 20 million anaesthetic prodecures.***

*AErrane™ (isoflurane) is not approved for use in obstetrics.

REFERENCES: 1. Cromwell TH, et al: Forane uptake, excretion and blood solubility in man. Anesthesiology 35:401-408, 1971. 2. Stevens WC, et al: The cardiovascular effects of a new inhalation anesthetic, Forane, in human volunteers at constant arterial carbon dioxide tension. Anesthesiology 35:8-16, 1971. 3. Linde HW, et al: Cardiovascular effects of isoflurane and halothane during controlled ventilation in older patients. Anesth Analg 54:701-704, 1975. 4. Mallow JE, et al: Hemodynamic effects of isoflurane and halothane in patients with coronary artery disease. Anesth Analg 55:135-138, 1976. 5. Lam AM, et al: Cardiovascular effects of isoflurane-induced hypotension for cerebral aneurysm surgery. Anesth Analg 62:742-748, 1983. 6. Levy W: Clinical evaluation of isoflurane: Cardiac arrhythmias. Can Anaesth Soc J 29 (suppl): 828-834, 1982. 7. Johnston RR, et al: A comparative interaction of epinephrine with enflurane, isoflurane and halothane in man. Anesth Analg 55:709-712, 1976. 8. Suzukawa M, et al: Use of isoflurane during resection of pheochromocytoma. Anesth Analg 62:100-103, 1983. 9. Adams RW, et al: Isoflurane and cerebrospinal fluid pressure in neurosurgical patients. Anesthesiology 54:97-99, 1981.

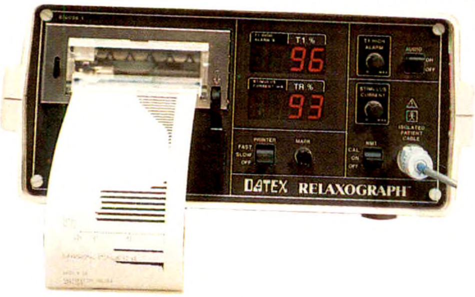
Prescribing Information. Indications: For general anaesthesia. **Dose:** Inspired concentrations of 1.5 to 3.0% AErrane produce surgical anaesthesia in 7 to 10 minutes. Surgical anaesthesia can be maintained with 1.0 to 2.5% AErrane when used concomitantly with nitrous oxide. **Contraindications:** Known sensitivity to AErrane or other halogenated anaesthetics; known or suspected genetic susceptibility to malignant hyperthermia. **Side Effects:** Hypotension, respiratory depression, arrhythmias, elevated white blood count, shivering, nausea, vomiting and ileus have been reported. **Product Licence Number:** 5247/0002.


© M.C. Escher Heirs c/o Cordon Art - Baarn - Holland

Draw your own conclusions

. . . about objective assessment of neuromuscular block with

THE RELAXOGRAPH –
NEUROMUSCULAR TRANSMISSION MONITOR



- Quantitative
- Automatic
- Non-invasive
- Continuous
- Reliable

For an early demonstration contact:
Nick Tyrrell, Product Manager, Vickers Medical,
Priestley Road, Basingstoke, Hants, RG24 9NP.
Telephone: 0256 29141

Vickers Medical

Microprocessor controlled 20s x T.O.F. stimulation gives digital TI + TR against calibrated values. An integral printer provides graphic account of changes in NMT.

Anaesthesia, 1986, Volume 41, pages 241–242

Editorial

A crisis of learning in anaesthesia

We, in the United Kingdom, use a system of preceptorship and apprenticeship to enable medical graduates both to acquire the loosely defined body of knowledge, and to develop the skills and attitudes necessary to practise anaesthetics. The opportunity for the student to see how the knowledge and skills are applied and to evaluate the results while learning the specialty are the advantages of this method. Learning from a tutor continues because it is successful, but it is nevertheless a system open to abuse. The anaesthetist in training must sometimes work alone, to practise what he has learned. But to leave him alone, overworked and perhaps tired, in situations which he does not fully understand seems to make a mockery of the whole system. Trainees need support and advice in proportion to their competence to manage the situations in which they find themselves, otherwise they will learn little.

There may be many reasons why this support and advice are not forthcoming. The junior doctor might not ask for help since he may be unaware of his own limitations and be overconfident, but the astute preceptor should know this. The hospital in which staffing arrangements require that the resuscitation of seriously ill or seriously injured patients is left to an anaesthetist inadequately trained to deal with them is much more worrying. If those who could both help and teach are already occupied in the intensive therapy unit or in an obstetrics department, there is little likelihood that the trainee will learn anything from the cases he is doing.

Our system of teaching by preceptor has become badly distorted. The increase in the amount of work in X ray departments and in day surgery units all too often means that anaesthetists in training anaesthetise patients by themselves; from this experience they learn very little because the skills and knowledge required to give the anaesthetic are beyond them. It is as clear to examiners for the Part I FFARCS, as it was to the DA examiners before them, that acceptable levels of anaesthetic practice are not learned by some trainee anaesthetists and that many have only a sketchy idea of the basic principles of resuscitation and of airway management which should be the foundation of anaesthetic teaching. The absence of understanding of the potential for danger in a given clinical scenario often shows up the deficiencies of instruction. The fact that the trainee has not personally experienced a problem and is therefore inclined to deny its existence tells us as much about the training as about the trainee. There is also evidence of the lack of immediate support for inexperienced anaesthetists who find themselves in deep trouble. These inadequacies simply ought not to occur in a proper training system based upon preceptorship.

This is a serious problem and it must first be recognised that our system of teaching anaesthetics demands that an experienced anaesthetist be available to work with and to teach each trainee. Instruction of totally inexperienced beginners by other members of the junior staff, who are themselves partially trained, is to perpetuate errors and half truths; both could be corrected were a senior person to be immediately present. More important, the pattern of anaesthetic practice, in which out of hours anaesthesia is left largely to unsupervised junior anaesthetists, deprives them of instruction when often it is most needed.

Teaching by preceptor has served anaesthesia well for many years and would need to be abandoned only if it were proved unworkable, which it clearly is not. We must, however, return to the principle upon which it is based: guidance and instruction are freely and constantly available to the learning anaesthetist. This may mean a change in the working habits of not only hospital anaesthetic departments, but also of individual senior anaesthetists. More consultants will be required to provide immediate support for inexperienced anaesthetists at all times. The financial and manpower changes necessary to meet this will have to be faced, but the results of such changes would be better training

0003–2409/86/030241 + 02 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

of the junior anaesthetists and fewer avoidable patient deaths. It is time we began to search for an acceptable solution to this problem.

Wexham Park Hospital,
Berkshire SL2 4HL

R.D. JACK

Editorial notices

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1**: 532–5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

News and Notices sections

The first issue of each quarter will contain full News and Notices sections.

Copy dates for these will be: 14 March 1986 for June 1986, 13 June 1986 for September 1986 and 12 September 1986 for January 1987.

Supplementary News and Notices sections will be published in other issues but they will contain only material which requires publication before the next full News and Notices section.

Stop press

Pain relief in labour: the benefits and risks

A national conference organised by the Maternity Alliance on 18 March in London for anaesthetists, midwives, mothers, obstetricians and paediatricians to discuss the different forms of pain relief available and their relative merits. Ring the Maternity Alliance on 01 388 6337 for further details.

Anaesthesia, 1986, Volume 41, pages 243–249

Plasma cholinesterase changes during the puerperium

N. ROBSON, I. ROBERTSON AND MARY WHITTAKER

Summary

Changes in plasma cholinesterase activity during the puerperium were studied in 16 women who received epidural analgesia for labour followed by vaginal delivery, and in five women who underwent elective Caesarean section under epidural analgesia. A consistent fall in cholinesterase activity was demonstrated during the first 2 to 3 days post partum, followed by a rise to approximately normal nonpregnant values by the end of the puerperium. An additional patient who manifested prolonged paralysis following an emergency Caesarean section under general anaesthesia, including a suxamethonium infusion, was also studied. Possible mechanisms by which the transient decrease in cholinesterase activity is produced, and its clinical significance, are discussed.

Key words

Enzymes; cholinesterase.
Anaesthesia; obstetric.

There are conflicting reports about the pattern of change in plasma cholinesterase activity during pregnancy,[1-5] but most workers have found that the rapid decline in activity which occurs during the first trimester produces significantly lower levels of activity in women during the second and third trimesters of pregnancy compared with nonpregnant populations.[2,3,6] Reports have shown that the lowest levels of activity occur in the first postpartum week,[2,3,5,7,] but changes on consecutive days in the same study have not been recorded. It has been shown that plasma cholinesterase activity in women returns to normal levels by the end of the puerperium.[8] The present study was designed to ascertain the pattern of recovery of plasma cholinesterase activity during the first 5 postpartum weeks, and to compare this pattern with that of plasma albumin concentration over the same period.

Methods

Two groups of women were studied. Group A consisted of 16 healthy pregnant women at term, who underwent spontaneous or induced labour with epidural analgesia, followed by vaginal delivery. Patients with any complication

---

N. Robson, MB, BChir, FFARCS, Senior Registrar, Department of Anaesthetics, City General Hospital, Newcastle Road, Stoke on Trent ST4 6QG, I. Robertson, BSc, MB, BCh, FFARCS, Registrar, Department of Anaesthetics, Gloucester Royal Hospital, Great Western Road, Gloucester GL1 3NN, Mary Whittaker, MSc, PhD, DSc, Chemistry Department, University of Exeter, Exeter, Devon EX4 4QD.

This work was carried out at Birmingham Maternity Hospital, Queen Elizabeth Medical Centre, Edgbaston, Birmingham.

0003–2409/86/030243 + 07 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

of pregnancy except mild pre-eclampsia were not studied, as were mothers of babies with any neonatal abnormality. None of the patients included had abnormal liver function or any major illness, and none received general anaesthetics. Venous blood samples were taken prior to the administration of epidural analgesia and subsequently at 4 days and 1, 2, 3 and 5 weeks postpartum.

To clarify changes in cholinesterase activity during the first postpartum week, a second group of five women (group B) was studied. All these patients were healthy and underwent obstetrically indicated elective Caesarean section under epidural analgesia. Blood samples were obtained from them prior to delivery and on days 1, 2, 3, 4, 5 and 42 postpartum.

Additionally, cholinesterase activity was assayed in a series of samples taken from another patient (patient C) who had an emergency Caesarean section for fetal distress under general anaesthesia, during which about 300 mg of suxamethonium was given by infusion to provide relaxation. Muscle paralysis persisted for about 20 minutes after the suxamethonium infusion was stopped at the end of the operation.

The study was explained to the subjects and verbal consent was obtained. Serum from the clotted blood samples was separated within a few hours of collection and stored frozen prior to estimation of cholinesterase activity and albumin concentration. Cholinesterase activity was assayed by the method of Kalow and Lindsay[9] and genotyped by measuring dibucaine[10] and fluoride numbers.[11]

Results

Fourteen of the subjects in group A were homozygous for the usual gene ($E_1^uE_1^u$) while two subjects were heterozygous for the silent and fluoride-resistant genes, $E_1^uE_1^s$ and $E_1^uE_1^f$,

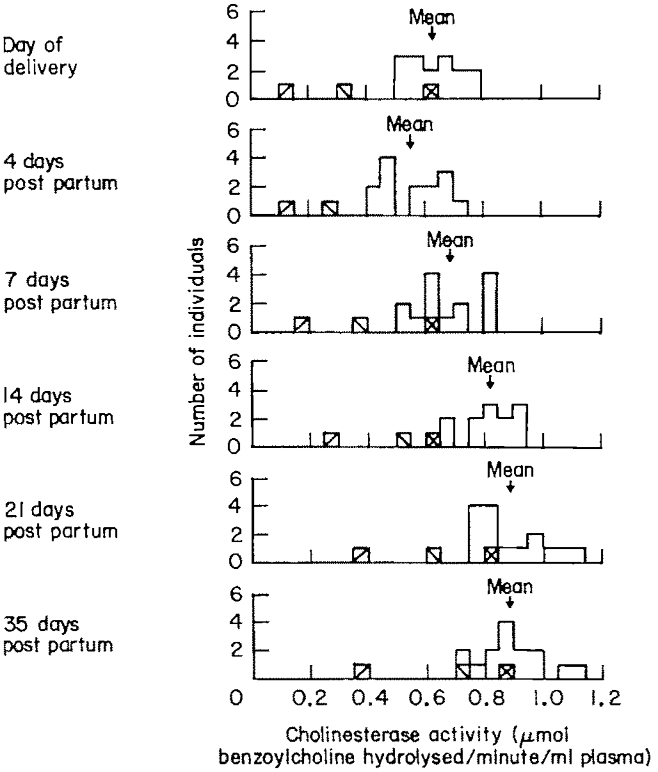


Fig. 1. Group A cholinesterase activities: (⧅), $E_1^uE_1^s$ heterozygote; (☒), $E_1^uE_1^f$ heterozygote; (⧄), $E_1^uE_1^s$ heterozygote (patient C). Mean values shown are for 14 patients with the usual genotype.

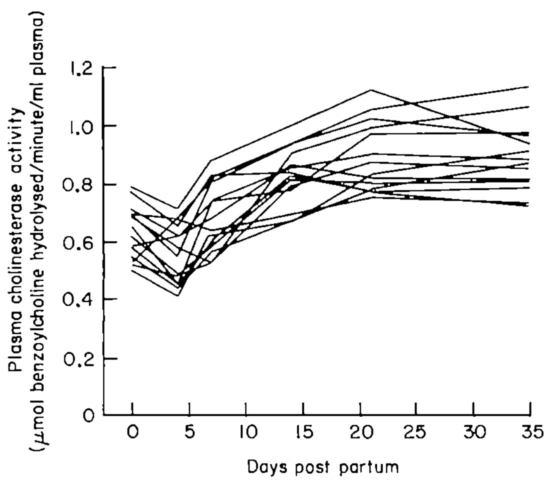


Fig. 2. Group A, $E_1{}^uE_1{}^u$ homozygotes (14 patients): individual plasma cholinesterase curves.

respectively. Cholinesterase activity data from these latter two patients are shown separately in Fig. 1, as are those from patient C who clinically manifested suxamethonium apnoea following an emergency Caesarean section. Patient C was heterozygous for the atypical gene ($E_1{}^uE_1{}^a$) with very low cholinesterase activity, which fell to only 0.1 units (micromol benzoylcholine hydrolysed/minute/ml plasma; normal nonpregnant range 0.80–1.20 units) during the first postpartum week and rose to just 0.37 units by the end of the puerperium. She was subsequently given a card from the Cholinesterase Research Unit in Exeter, warning of her sensitivity to suxamethonium. Her baby was investigated at 6 weeks of age and found to have the usual genotype with normal cholinesterase activity.

Excepting those subjects with unusual genotypes, there was fairly wide between-patient variation in plasma cholinesterase activity within group A, as predicted by the flat Gaussian distribution curve of activities obtained when randomly screening a healthy population of Caucasian adults. The pattern of change in activity in each patient was more constant, as illustrated by Fig. 2. The mean level of cholinesterase activity at delivery was about 30 percent less than that found at 5 weeks postpartum and fell during the first post partum week to nearly 40 percent less, rising to approximate the delivery level by the end of the first postpartum week. Mean cholinesterase activity then rose to reach the 5-week value 2 weeks later. Changes in albumin concentration followed a similar pattern (Fig. 3).

Of the 14 subjects in group A with the usual genotype, 4 (29 percent) had cholinesterase activities 4 days postpartum that were 50 percent or less than the 5 weeks postpartum value. The range of values of cholinesterase activity in these patients at delivery was 0.5–0.79 units. Four days postpartum, the range of values was 0.41–0.71 units, with six subjects (43 percent) having values less than 0.5 units and at 3 weeks postpartum the range was 0.75–1.12 units. Ten of these 14 subjects (71 percent) had cholinesterase activities within the normal nonpregnant range 3 weeks postpartum and eleven (79 percent) fell within the normal range 5 weeks postpartum.

The $E_1{}^uE_1{}^a$ variant occurs with an incidence of about 0.5 percent in a Caucasian population and it is of note that the cholinesterase activity of the $E_1{}^uE_1{}^a$ heterozygote studied here fell to a very low level (0.28 units) during the first postpartum week, but rose to lie within the range of values of the $E_1{}^uE_1{}^u$ homozygotes by the fifth postpartum week, with a value of 0.75 units, representing an increase in activity of 269 percent.

Group B similarly showed fairly wide between-patient variation in cholinesterase activity, especially of 6 weeks postpartum values. In all five patients in this group, the level of cholinesterase activity fell to a single lowest value on the second, third or fourth day postpartum and was rising again by the fifth postpartum

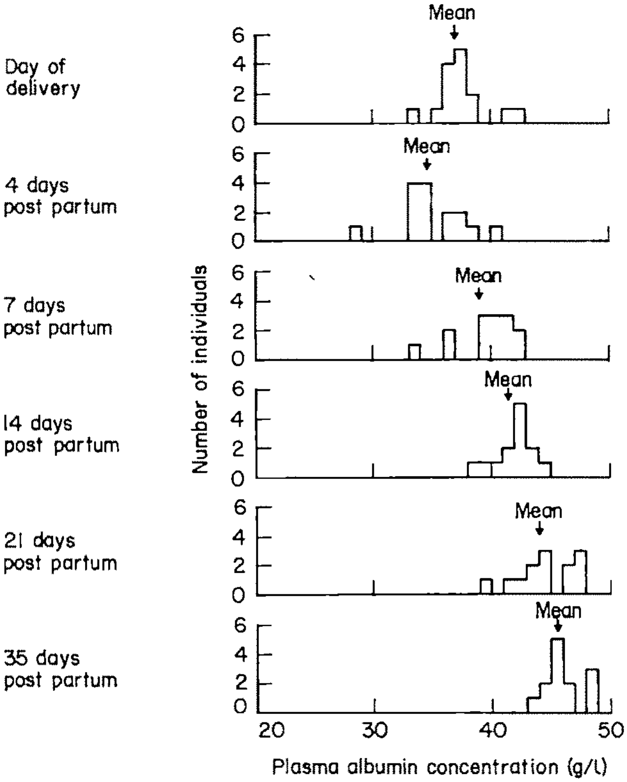


Fig. 3. Group A, plasma albumin concentrations with mean values.

day. The range of the lowest values was 0.37–0.48 units (Fig. 4).

Discussion

It is apparent from our results that maternal plasma cholinesterase activity decreases during the early puerperium and, on average, reaches a minimum at about 3 days following parturition. A similar decrease in plasma albumin also occurs during this period. These plasma proteins subsequently show a progressive increase in concentration until nonpregnant values are observed, often at 3 weeks postpartum. A few patients show a slower recovery, taking 5–6 weeks to reach the nonpregnant values for these proteins.

The cause of the decrease in these proteins demands an explanation since de Alvarez[12] has shown that the alpha$_1$ globulins, unlike albumin and cholinesterase, show little variation from the nonpregnant control until delivery, when a marked transitory rise occurs during the early puerperium. De Alvarez and his colleagues[12] have not only examined the changes in serum protein fractionation which occur during pregnancy, but also the analogous changes of the same proteins found in other clinical conditions. For example, they found that nephrosis has, like pregnancy, depressed albumin and gamma globulin levels with elevated fibrinogen. Plasma cholinesterase activity is significantly elevated in the nephrotic syndrome,[13] in contrast to the decreased activity observed during pregnancy and the early puerperium. This discrepancy in plasma albumin and cholinesterase chemistry is not surprising, since albumin (a small protein with a molecular weight of 69000) is excreted by the damaged tubules, whereas cholinesterase (molecular weight 3 × 10^5) is retained by the tubules in nephrosis.

Albumin, like plasma cholinesterase, is biosynthesised in the liver, but the blood chemistry of the two proteins can differ, thus, in analbuminaemia, patients have normal plasma cholin-

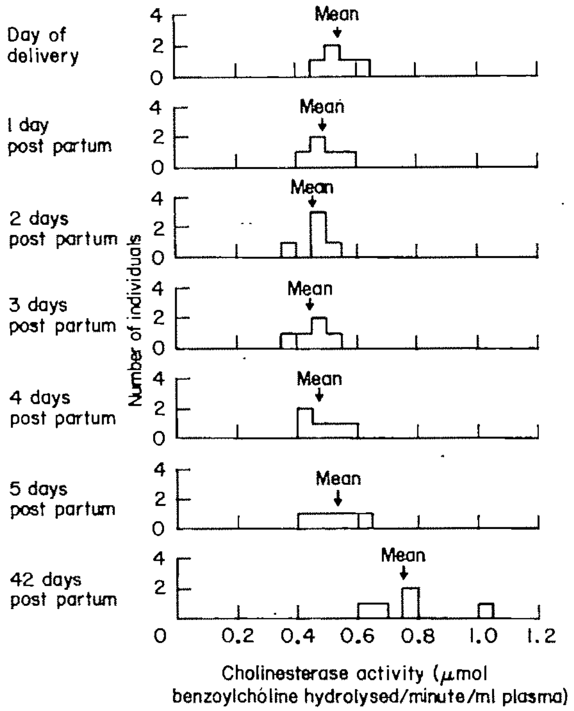


Fig. 4. Group B, cholinesterase activities with mean values.

esterase levels[14] whilst a Bantu girl lacking cholinesterase in her plasma had a normal serum albumin level.[15] However, our observations of the decreased albumin and cholinesterase in the early puerperium suggest that the explanation of both results is probably identical. There is a rapid loss of plasma fluid during the first few days after delivery,[16] when as much as 50 percent of the total postpartum plasma volume loss occurs; normal nonpregnant levels are attained in 6–9 weeks. The characteristic postpartum diuresis does not account for the total plasma volume loss, indicating that some of the fluid must be lost into the tissues as evidenced by the oedema of hands and feet frequently observed in mothers on about the third postpartum day. However, loss of plasma volume, either by diuresis or by osmotic process into tissues, should produce an increase in the concentration of the two plasma proteins as is observed with alpha globulins.[12] It is remarkable that the minimum cholinesterase activity and albumin concentration coincide with maximum plasma volume decrease.

It has been suggested that the steroids may produce a slight increase in the permeability to proteins. Such a hypothesis could explain the decrease in serum albumin and would support the observations of Laurell *et al.*[17] that gammaG and gammaM levels do not change during the immediate postpartum period, but it does not explain the decreased cholinesterase activity if molecular weight dimensions of the protein are to be considered.

With the exception of the immunoglobulins, the plasma proteins are mainly synthesised in the liver. The concept of a steroid-induced depression of the liver's ability either to synthesise a protein or to release it, lacks support from metabolic studies. However, Doe *et al.*[18] indicate that oestrogens have a stronger inductive effect on protein synthesis than any other steroid, although the effect of oxytocin has not, to our knowledge, been examined. Supportive evidence that the observed changes in plasma proteins can, in part, be attributed to modified steroid metabolism during pregnancy, arises from consideration of oestrogen–protesterone containing contraceptives which promote similar changes in plasma proteins.[2,17] The changes in serum albumin and cholinesterase are reversed on withdrawal of the contraceptive,[19,20] but to our knowledge the early changes during the first 5 days after withdrawal have not been observed.

Oestrogens are present in plasma, partly in the free form and partly conjugated; about 50–75 percent are bound to plasma proteins, mainly gammaglobulin. During the last 2 weeks of gestation, a rapid conversion of combined to, free oestrogen has been reported. After delivery of the placenta, oestrogen is rapidly cleared from the blood and is not usually demonstrable after the third day. Although it is tempting to suggest that the diminished cholinesterase activity observed during pregnancy and the early puerperium could be the result of the known powerful inhibiting effect of many steroid derivatives,[21] in the light of its negligible concentration in plasma on the third day postpartum, the effect of oestrogen in this role is untenable. However, on a similar tack, plasma cortisol increases during the third trimester of pregnancy as well as during administration of oestrogens. While 95 percent of the normal concentration of plasma cortisol is bound to one or more alpha globulins, at elevated concentrations 70–80 percent of the increment is bound to albumin, the remainder being unbound. If the cortisol—albumin conjugated protein blocked the active site of plasma cholinesterase, then we could account for the decreased albumin and cholinesterase activities. Such a suggestion at this stage is speculative. It is apparent that one must measure the molar concentration of the enzyme by immunoassay in order to determine whether enzyme induction or inhibition is the probable explanation for the observed changes in cholinesterase activity during the puerperium, since in our opinion, plasma volume changes are not relevant.

A number of workers have investigated the relationship between plasma cholinesterase activity and the duration of action of suxamethonium. Walts *et al.*[22] found a three-fold increase in the duration of apnoea produced by suxamethonium when plasma cholinesterase activity was 25 percent of normal, while in a population of pregnant women with cholinesterase activities greater than 50 percent of normal, Blitt and his colleagues[7] could find no correlation between cholinesterase activity and the duration of suxamethonium apnoea. In a study of individuals with the genotypically normal enzyme, Viby-Mogensen[23] demonstrated a linear relationship between the inverse of plasma cholinesterase activity and the duration of suxamethonium apnoea or the time to 100 percent recovery of twitch height produced by nerve stimulation. Evans and Wroe[24] analysed blood samples from 250 normal and suxamethonium-sensitive individuals and demonstrated that a cholinesterase activity 2.5 standard deviations below the mean normal activity of $E_1{}^{u}E_1{}^{u}$ individuals identifies over 90 percent of suxamethonium-sensitive individuals. The value of cholinesterase activity 2.5 standard deviations below mean normal cholinesterase activity of heterozygotes for the usual gene approximated to 50 percent of normal activity.

It is apparent from our study that cholinesterase activity is significantly reduced during the first 3 postpartum weeks and, especially during the first postpartum week, a relatively greater proportion of women given suxamethonium could be expected to exhibit prolonged paralysis than in an equivalent nonpregnant population. This expectation is not, however, borne out by experience at the Birmingham Maternity Hospital, where women undergoing Caesarean section under general anaesthesia routinely receive large doses of suxamethonium by infusion without an obviously high incidence of prolonged paralysis. We suggest that while careful vigilance for suxamethonium apnoea is appropriate when the drug is used during the puerperium, the risks of inadequate relaxation for intubation make reduction of suxamethonium dosage unjustifiable.

Acknowledgments

The authors gratefully acknowledge the advice and encouragement of Dr J. S. Crawford and financial assistance to M.W. from the Sir Halley Stewart Trust.

References

1. SHNIDER SM. Serum cholinesterase activity during pregnancy, labor and the puerperium. *Anesthesiology* 1965; **26**: 335–9.
2. ROBERTSON GS. Serum cholinesterase deficiency. II, Pregnancy. *British Journal of Anaesthesia* 1966; **38**: 361–9.
3. EVANS RT, WROE JM. Plasma cholinesterase changes during pregnancy. Their interpretation as a cause of suxamethonium-induced apnoea. *Anaesthesia* 1980; **35**: 651–4.

4. Meade BW, Rosalki SB. Serum enzyme activity in normal pregnancy and the newborn. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 1963; **70:** 693–700.
5. Hazel B, Monier D. Human serum cholinesterase: variations during pregnancy and post-partum. *Canadian Anaesthetists' Society Journal* 1971; **18:** 272–7.
6. Levine MG, Hoyt RE. Serum cholinesterase in some pathological conditions. *Proceedings of the Society of Experimental Biology and Medicine* 1949; **70:** 50–3.
7. Blitt CD, Petty WC, Alberternst EE, Wright BJ. Correlation of plasma cholinesterase activity and duration of action of succinylcholine during pregnancy. *Anesthesia and Analgesia* 1977; **56:** 78–83.
8. Piccoli R, Longo G. La colinesterasi serica in ostetrica: valori della C.S. nella gravidanza normale. (Serum cholinesterase in obstetrics: values in normal pregnancies.) *Bollettino Societa Italiana di Biologia Sperimentale* 1947; **23:** 353–5.
9. Kalow W, Lindsay HA. Comparison of optical and manometric methods for assay of human serum cholinesterase. *Canadian Journal of Biochemistry and Physiology* 1955; **33:** 568–74.
10. Kalow W, Genest K. A method for the detection of atypical forms of human serum cholinesterase: determination of dibucaine numbers. *Canadian Journal of Biochemistry and Physiology* 1957; **35:** 339–46.
11. Harris H, Whittaker M. Differential inhibition of human serum cholinesterase with fluoride: recognition of two new phenotypes. *Nature* 1961; **191:** 496–8.
12. De Alvarez RR, Alfonso JF, Sherrard DJ. Serum protein fractionation in normal pregnancy. *American Journal of Obstetrics and Gynecology* 1961; **82:** 1096–111.
13. Kunkel HG, Ward SM. Plasma esterase activity in patients with liver disease and the nephrotic syndrome. *Journal of Experimental Medicine* 1947; **86:** 325–37.
14. Dietz AA, Rubenstein HM, Lubrano T. Serum cholinesterase in analbuminemia. *Clinical Chemistry* 1966; **12:** 25–7.
15. Jenkins T, Balinsky D, Patient DW. Cholinesterase in plasma: first reported absence in the Bantu; half-life determination *Science* 1967; **156:** 1748–50.
16. Lund CJ, Donovan JC. Blood volume during pregnancy. Significance of plasma and red cell volumes. *American Journal of Obstetrics and Gynecology* 1967; **98:** 393–403.
17. Laurell CB, Kullander S, Thorell J. Effect of administration of a combined estrogen—progestin contraceptive on the level of individual plasma proteins. *Scandinavian Journal of Clinical Laboratory Investigation* 1968; **21:** 337–43.
18. Doe RP, Mellinger GT, Swaim WR, Seal US. Estrogen dosage effects on serum proteins: a longitudinal study. *Journal of Clinical Endocrinology and Metabolism* 1967; **27:** 1081–6.
19. Whittaker M, Charlier AR, Ramaswamy S. Changes in plasma cholinesterase isoenzymes due to oral contraceptives. *Journal of Reproduction and Fertility* 1971; **26:** 373–5.
20. Redderson CL. Interactions of steroids and serum cholinesterase. *International Journal of Clinical Pharmacology, Therapy and Toxicology* 1973; **8:** 51–7.
21. Whittaker M, Britten JJ. Inhibition of the plasma cholinesterase variants by pancuronium bromide and some of its analogues. *Clinica Chimica Acta* 1980; **108:** 89–94.
22. Walts LA, Dillon JB. Clinical studies on succinylcholine chloride. *Anesthesiology* 1967; **28:** 372–6.
23. Viby-Mogensen J. Correlation of succinylcholine duration of action with plasma cholinesterase activity a predictor of succinylcholine sensitivity? enzyme. *Anesthesiology* 1980; **53:** 517–20.
24. Evans RT, Wroe J. Is serum cholinesterase activity a predictor of succinyl choline sensitivity? An assessment of four methods. *Clinical Chemistry* 1978; **24:** 1762–6.

Anaesthesia, 1986, Volume 41, pages 250–257

Diabetes mellitus and open heart surgery

A simple, practical closed-loop insulin infusion system for blood glucose control

B. G. WATSON, M. J. ELLIOTT, D. A. PAY AND M. WILLIAMSON

Summary

A method, based on bedside determinations of blood glucose by nursing staff, was designed to control the administration of insulin to diabetic patients during and following open heart surgery. A computer-controlled intravenous infusion pump was used to deliver the insulin. Excellent control of the hyperglycaemia normally associated with open heart surgery was achieved, with 84 percent of measured blood glucose values falling within 2 mmol/litre of the target value of 6 mmol/litre. The method proved to be simple, effective, and safe.

Key words

Surgery; cardiac.
Metabolism; diabetes mellitus, insulin.
Monitoring; blood glucose.

Operations involving cardiopulmonary bypass are particularly liable to produce severe metabolic disturbances in the diabetic patient.[1] Insulin requirements are higher than for other procedures. Hyperglycaemia can be controlled by infusing insulin and, if this is done, the metabolic disturbances can be minimised.[1]

Both automated (Biostator artificial pancreas) and manual (operator control of insulin infusion rate) feedback methods have been used at the time of open heart surgery to maintain blood glucose concentrations within acceptable limits.[2] Both these techniques have disadvantages. The Biostator although very effective is complex, labour-intensive, and needs close medical and technical supervision and a continuous flow of blood. It is expensive and thus not available in many units. A technique using periodic blood glucose estimations and manual control of an insulin infusion is impractical in many clinical situations. Considerable experience is necessary to alter the insulin infusion rate appropriately during the rapid fluctuations of blood glucose concentration (due to variations of insulin resistance and endogenous glucose production) which may be encountered.[3] Control is needed for long periods, and frequently requires skilled attention.

We present a solution to these problems which can be operated by the nurse at the bedside with a reflectance meter. It can be used in two forms. One uses a computer-controlled insulin pump and a modified Reflocheck (Boehringer-Mannheim) blood glucose meter. The other uses

---

B.G. Watson, MB, BS, FFARCS, Consultant Cardiothoracic Anaesthetist, D.A. Pay, BSc (Hons), Principal Physicist, M. Williamson, BSc (Hons), Physicist, Regional Cardiothoracic Centre and Regional Medical Physics Department, Freeman Hospital, High Heaton, Newcastle on Tyne NE7 7DN, M.J. Elliott, MD, FRCS, Senior Registrar in Paediatric Cardiac Surgery, Hospital for Sick Children, Great Ormond Street, London WC1N 3JH.

0003–2409/86/030250 + 08 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

a simple table showing by how much a manually controlled insulin pump should be altered in given circumstances. The two systems are identical in that they use the same set of instructions. In both systems, the user measures the blood glucose concentration with the Reflocheck. In one system, the insulin pump is then altered manually by the user according to the table. In the other, the calculation and alteration of the insulin infusion rate are performed automatically.

Patients and methods

Patients

Twelve unselected diabetic patients having open heart surgery were studied (Table 1). They were taken from the group of 13 consecutive diabetics operated upon between August 1984 and January 1985. The single patient not studied was not known to be diabetic until immediately before the operation. Informed consent was obtained from all patients.

Ten patients were male and two were female. They were aged between 39 and 64 years (mean 54.6 years) and weighed between 56 and 85 kg (mean 69 kg). Diabetic control pre-operatively was with diet alone in three, with oral hypoglycaemic agents in six, and with insulin in three. Coronary artery bypass grafting was performed in nine patients (one for the second time), emergency repair of a ventricular septal defect (VSD) and coronary artery bypass grafting following myocardial infarction in one, replacement of a mitral prosthesis in one, and suture of a secundum atrial septal defect in one.

Oral hypoglycaemic agents were stopped the day before operation and all patients were starved overnight. No patient was considered to be so insulin-dependent that overnight glucose/insulin/potassium was required. The morning dose of insulin was omitted. Benzodiazepine (temazepam or lorazepam) premedication was given orally one hour before operation. Induction and maintenance of anaesthesia were according to the preference of the anaesthetist; no attempt was made to influence this. The principal induction agent was fentanyl, and all patients were paralysed with pancuronium. A variety of agents were used to supplement nitrous oxide anaesthesia and to control the blood pressure. No glucose was given during the operation, and the oxygenator priming solution contained no blood, glucose, or lactate as recommended by Elliott *et al.*[2] After induction of anaesthesia, an insulin infusion at either 5 or 10 units/hour was started through a dedicated cannula. Control of the insulin infusion rate was then passed to the computerised system (see below). Blood glucose estimations were performed by the anaesthetist at intervals of 15 minutes throughout the operation.

At the end of the procedure, the data were stored on disk and the computer switched off during transfer of the patient to the intensive care unit. The insulin pump was then restarted and control of its rate was again passed to the computer. An infusion of glucose was started at a rate of 0.1 g/kg body weight/hour. This was continued until the patient left the intensive care unit. The rate at which the insulin infusion was restarted took into account this glucose load provided that the last blood glucose concentration in the theatre had not been low, the insulin

Table 1. Details of patients studied

Patient	Age (years)	Sex	Weight (kg)	Diabetes	Procedure	Outcome
B F	39	M	74	NIDDM	Patch ASD	Discharged 9th postop day
A T	52	M	75	NIDDM	CAVG × 7	Discharged 6th postop day
A McG	51	F	57	NIDDM	Redo MVR	Died on 65th postop day
J P	55	M	72	NIDDM	Redo CAVG × 4	Discharged 11th postop day
W C	62	M	73	NIDDM	CAVG × 6	Discharged 13th postop day
R H	52	F	60	NIDDM	CAVG × 6	Discharged 13th postop day
R G	62	M	70	IDDM	CAVG × 6	Discharged 10th postop day
A H	64	M	70	NIDDM	CAVG × 1, VSD	Died on 20th postop day
W K	57	M	85	NIDDM	CAVG × 4	Discharged 14th postop day (renal failure, PD)
M F	57	M	73	NIDDM	CAVG × 7	Discharged 22nd postop day
A S	57	M	65	IDDM	CAVG × 7	Discharged 7th postop day
V T	47	F	56	IDDM	CAVG × 3	Died on 2nd postop day

(N) IDDM = (non) insulin-dependent diabetes mellitus; PD = peritoneal dialysis.

was restarted at a rate approximately 50 percent higher than before.

Most patients left the intensive care unit on the day after surgery. Computer control was stopped shortly before transfer to the general ward. An infusion of glucose, insulin, and potassium was started with a ratio of glucose to insulin the same as had been given over the preceding 4 hours. Data on further management are not presented here.

Manual control of the insulin infusion rate

This was used to control the insulin infusion rate in one patient after the computer keyboard had been damaged accidentally. A simple table (Table 2) was used. This was evolved during pilot studies over the previous two and a half years and was based on the difference between consecutive values of the blood glucose. Blood samples were taken from the arterial cannula used for blood pressure monitoring, and glucose content estimated immediately using a Reflocheck. The Reflocheck was chosen for its known ease of use, accuracy, and reliability.[4] The blood glucose result was rounded down to the nearest whole number of millimoles. If the result was very high (> 15 mmol/litre) the estimation was repeated before proceeding. The insulin infusion rate was then altered according to the number (the 'factor') obtained from the table by consulting the row and the column determined by the previous, and the most recent, blood glucose values respectively. The insulin infusion rate was multiplied by the adjustment factor to obtain the new rate. The insulin infusion pump was then set to this rate.

Table 2. Chart of instructions for users of the manual system. The user measures the blood glucose concentration using the Reflocheck, and rounds down the result to the nearest whole number. The table is then consulted, using the row and column determined by the previous and the most recent blood glucose respectively, and finds the 'factor'. The current insulin infusion rate is then multiplied by the factor to find the new value. The user then sets the insulin pump to this rate. The text shows safety checks which are made before the insulin pump is altered.

Last result	This result							
	1 or 2	3	4	5	6	7	8	9 or over
1 or 2	0*	Give 2 units/hour				Give 5 units/hour		
3	0*	0.25	0.5	1	1.5	2	2.5	3
4	0*	0.25	0.5	1	1.5	2	2.5	3
5	0*	0.25	0.5	0.75	1.25	2	2.5	3
6	0*	0.25	0.5	0.5	1	1.5	2	3
7	0*	0.25	0.3	0.5	0.8	1.5	2	2.5
8	0*	0.1	0.25	0.5	0.75	1	2	2.5
9 or over	0*	0.1	0.1	0.5	0.5	0.75	1.5	1.5

—Half-hourly Reflocheck B.G. estimations
—if result over 15 mmol/l, repeat to confirm before proceeding
—round result down to nearest whole number
—using this result and last result, consult table to find factor
—multiply old insulin rate by factor to get new insulin rate
—if new rate is 80 U/hr or over, new rate is 80 U/hr
—change insulin infusion rate
—if factor is in a stippled square, change to ¼ hrly estimations
*Give 20 ml of 50% dextrose intravenously and reduce insulin to minimum rate.

The interval between blood samples was 15 minutes during operation, and 30 minutes postoperatively. The latter interval was shortened if the derived factor was found to be in a stippled square on the table. This would occur when the blood glucose was low, when it had changed by a large amount over the previous sample period, or when it was high and the insulin infusion rate needed to be increased rapidly. The sample interval was then reduced to 15 minutes until the new factor was no longer in a stippled square.

An arbitrary upper limit of 80 units/hour was set on the insulin infusion rate; this was never exceeded. A lower limit was set according to the pre-operatively assessed severity of the diabetes: 2 units/hour for those who were insulin-dependent pre-operatively, 1 unit/hour for those on oral hypoglycaemic agents, and 0.5 units/hour for those who were controlled by diet alone. If a blood glucose concentration of less than 3.0 mml/litre was measured, 20 ml 50% dextrose was given intravenously and the insulin infusion rate reduced to the minimum level. There were no additional instructions to correct or prevent anticipated changes caused by the administration of blood or inotropic agents.

Computer control of the insulin infusion rate

A microcomputer-based system (Fig. 1) was developed, in conjunction with the Regional Medical Physics Department, to control the rate of the insulin infusion according to the instructions used in the manual system described above. It was used to control the insulin administration to 11 of the 12 patients studied, both during operation and postoperatively. Blood samples were taken at intervals of 15 or 30 minutes as above, and analysed immediately using a Reflocheck blood glucose meter, modified by the addition of an interface to an Apple II microcomputer which monitored the blood glucose concentration result. The computer used this result and the previous blood glucose value to derive the appropriate factor from the table, calculated the new insulin infusion rate and set the insulin pump automatically to this rate for the following period.

The software was designed so that after initial set-up, the minimum of attention was required from the operator. The normal operating mode of the system was to display graphically the most recent 12 hours' values of blood glucose concentration, and insulin and glucose infusion rates (Fig. 2). The lower part of the screen showed, in text form, the current values, and a moving cursor indicated that the system was working. A menu was available at the press of a key, so that manual alterations of parameters could be made, or hard copy obtained.

Two modified Imed 927 infusion pumps were connected to the computer via an interface box. One was monitored by the computer and delivered an infusion of dextrose; the other was controlled, and infused Actrapid monocomponent insulin 1 unit/ml polygeline. Although manually adjustable only in increments of 1 ml/hour, the insulin pump could be controlled in steps of 0.1 ml/hour by being electrically switched rapidly between higher and lower rates. Computer control was only possible when the pump flow rate control was set to zero. Manual override was thus possible at any time, simply by setting a pump rate of more than zero.

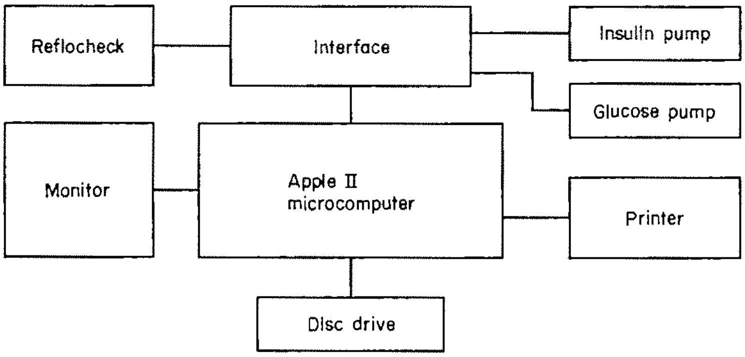
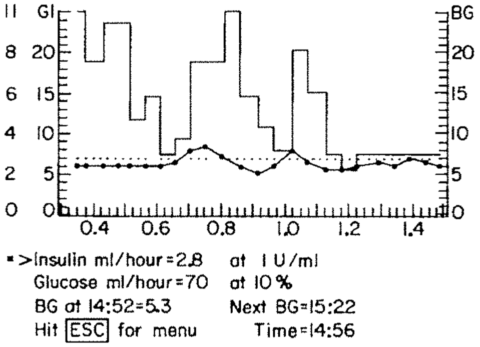


Fig. 1. The layout of the computerised system.



```
• >Insulin ml/hour=2.8    at  1 U/ml
   Glucose ml/hour=70     at 10 %
   BG at 14:52=5.3        Next BG=15:22
   Hit [ESC] for menu       Time=14:56
```

Fig. 2. The appearance of the monitor screen while the system is running. If an alarm condition occurs, or to give instructions to the user, the graphical display is cleared. The cursor (= >) moves between the first three lines of text as an indication that the system is working. . . . . ., Glucose infusion rate (GI) g/hour; ●—●, blood glucose concentration (BG) mmol/litre; ⌐, insulin rate (II) units/hour.

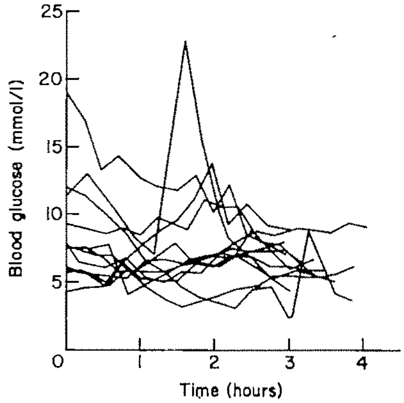


Fig. 3. Blood glucose concentrations during operation. Values for all 12 patients are shown. Zero time is the time of the first blood glucose estimation, shortly after induction of anaesthesia. The single very high peak occurred after a bolus of dextrose had been given in error.

A comprehensive set of inbuilt safety checks was made at intervals of, on average, 2 seconds. Flashing alarm messages or prompts were displayed, with an audible tone, in the area of the computer screen normally occupied by the graphical display, to alert the user to the following conditions: estimation due shortly, estimation overdue, insert stick into Reflocheck, manual over-ride of insulin pump (e.g., setting of a non-zero rate), pump switched off, or connexions between computer and pump broken (e.g., plug out, broken wire), insulin or glucose pump alarm condition (e.g., line blocked, air in line, low battery; in the case of the insulin pump, the pump was stopped until the cause of the alarm had been removed and the pump reset), change in insulin strength required (insulin concentration was increased if the volume infusion rate exceeded 30 ml/hour, to avoid the administration of excessive volumes. It was decreased if less than 2 units/hour were being given with a concentration of more than 1 unit/ml), error in Reflocheck (e.g., low battery if the mains power supply was not in use, or internal electronic fault), interface box power supply failure, software error.

If the computer power supply failed, the insulin pump stopped, the computer screen became blank and an audible, battery powered alarm sounded. It was never considered necessary to interfere with the computer's management of the insulin infusion by manually setting a different rate from that calculated by the computer.

Results

Blood glucose concentrations during operation (Fig. 3) were within 2 mmol/litre of the target value of 6 mmol/litre in 65.7 per cent of samples. The mean value was 7.5 (SD 0.7) mmol/litre. Postoperatively, in the intensive care unit, 88 percent of samples were within 2 mmol/litre of the target value (Fig. 4). The mean value was 6.3 (SD 0.5) mmol/litre. Overall, 82.2 percent of results fell within the desired range.

Insulin infusion rates during operation (Fig. 5) varied from 0.5 to 80 units/hour. Postoperatively (Fig. 6), up to 80 units/hour were given. Blood glucose concentrations of less than 4.0 mmol/litre occurred on 15 occasions; in eight out of 172 estimations during operation, and in seven out of 480 estimations postoperatively. Six of these 15 results were from one patient, a 62-year-old, insulin-dependent patient who had a coronary artery bypass graft. This patient also had the lowest single value recorded, of 2.1 mmol/litre. The highest single value of 22.8 mmol/litre was found immediately after 500 ml 5% dextrose had been given during operation, as a result of operator error.

There were no intra-operative deaths. Three patients died after operation. One patient, a 51-year-old woman with a malfunctioning mitral prosthesis had a protracted postoperative course with hepatorenal failure and died 65 days postoperatively. A second patient, a 64-year-old man

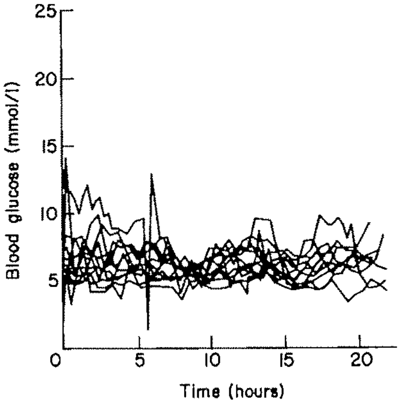


Fig. 4. Blood glucose concentrations postoperatively. Zero time is the time of the first estimation on arrival in the intensive care unit. The lowest single value shown was caused by operator error (see text) and was followed by a much higher peak when the operator gave 20 ml 50 percent dextrose intravenously, following the instruction given by the computer which had registered an erroneous value of 1.1 mmol/litre.

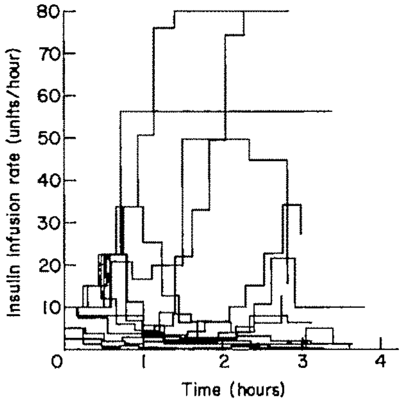


Fig. 5. Insulin infusion rates during operation. Values for all 12 patients.

who had the emergency repair of VSD and a coronary artery bypass graft, following a myocardial infarction, died 20 days after operation of persistent left ventricular failure. A third patient, a 47-year-old woman with severe generalised arterial disease and end-stage renal failure left the intensive care unit the day after a coronary artery bypass graft but suffered further subendocardial infarction during the following night, and died in intractable ventricular fibrillation.

Eight of the 12 patients left the intensive care unit on the day following surgery, one left on the second, and one on the third postoperative day. Survivors were discharged from hospital between 6 and 22 days postoperatively (mean 10 days).

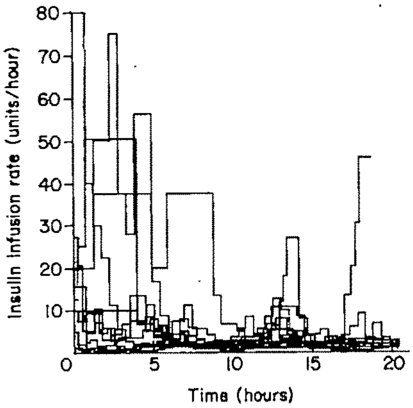


Fig. 6. Insulin infusion rates postoperatively. Values for all 12 patients.

Technical difficulties were very rare. One estimation in the intensive care unit produced a blood glucose result of 1.1 mmol/litre after too vigorous wiping of the reagent stick had abraded most of the surface layer, and exposed the white backing material to cause an incorrect value. The patient was given 20 ml 50% glucose intravenously in accordance with the alarm message displayed by the computer as a result of the 'hypoglycaemia'.

Discussion

The metabolic response to surgery and anaesthesia includes increased secretion of cortisol, catecholamines, glucagon and growth hormone, and inhibition of insulin secretion. There is increased mobilisation of gluconeogenic precursors, particularly amino acids, increased protein degradation, gluconeogenesis, glycogenolysis, with enhanced lipolysis and insulin resistance.[1] These changes all lead to hyperglycaemia, which, in the insulin-dependent diabetic patient, may be severe and accompanied by ketoacidosis. In the non-insulin-dependent diabetic patient, there may be milder changes due to the inability to generate appropriately high insulin secretion rates and the presence of insulin resistance.

The desirability of maintaining good control of diabetes at the time of major surgery is well established. It is certainly as desirable during and after open-heart surgery. One study has shown that, at the time of open heart surgery, diabetic patients who were well controlled using a Biostator, when compared with those in whom this was not used, showed a decreased incidence of dysrhythmias and low output syndrome, less difficulty with weaning from cardiopulmonary bypass, but were more prone to postoperative hypertension.[5] Operations involving cardiopulmonary bypass are associated with large increases in insulin requirements. Normoglycaemia can be maintained by insulin infusion, and metabolic acidosis, ketone body production, gluconeogenesis, and lipolysis can be prevented.[2,6]

The blood glucose concentration can be controlled very accurately by using the Biostator. It is not, however, a practical clinical tool. The alternative, the use of a manually controlled insulin pump, requires close skilled attention because insulin resistance and endogenous glucose production may change rapidly by large amounts.[2] The method we describe overcomes these difficulties. The initial aim of the study was to develop a set of instructions in the form of a chart, to help nursing staff to alter the insulin infusion rate appropriately in response to bedside blood glucose estimations. The magnitude of each of the factors in the chart (Table 2) and the range of blood glucose values to which it refers, were first set empirically, and have been altered subsequently to their present values as a result of experience using the method with a manually controlled insulin infusion. It was to assess the method in this manual form that the computer-controlled system was developed. The same factors used in the chart are used by the computer system. Other considerations were that the sample timing, arithmetical and rate-setting errors, which are made occasionally when the method is used manually, should be avoided. The manual system was designed to be as simple as possible because it may be used in units without access to the computer-controlled system. It is simple enough to fit on one side of A4 paper and can be used without prolonged training by nursing staff equipped with a pocket calculator.

The target value for the blood glucose was, like the values of the factors in the chart, first set arbitrarily, since there is little agreement on the most desirable level. Our initial aim in earlier studies using the manual method was to keep the blood glucose between 7 and 10 mmol/litre, a compromise between avoiding excessive hyperglycaemia while being quite safe from hypoglycaemia. The use of the chart reduces the insulin infusion rate, whenever the blood glucose is low or falling rapidly, much more rapidly than it ever increases it, in order to avoid hypoglycaemia. Experience showed that hypoglycaemia was very infrequent, and for the present study a lower target value of 6 mmol/litre was chosen. Hypoglycaemia has not been troublesome.

The degree of accuracy achieved in control of the blood glucose in our study has been encouragingly high, with 66 percent of blood glucose concentration results during operation, and 88 percent of values postoperatively, falling between 4 and 8 mmol/litre. The quality of control was even better than that achieved by Elliott *et al.*[2] or Kuntschen *et al.*,[5] both of whom used much more elaborate systems. Of the results quoted by Bowen *et al.*[7] during minor surgery and obstetrical procedures with insulin-dependent patients, only 28.6 percent of values were within our target range of 4–8 mmol/litre. Forty-six percent were within their target range of 5–10 mmol/litre achieved by using glucose/insulin/potassium solutions and measuring the blood glucose hourly. Even worse results have been reported by Gill *et al.*[8] in control of diabetes mellitus during open heart surgery.

The hospital mortality of three patients out of twelve is high for the types of procedure involved. We do not, however, believe that this is related to the diabetic control; only one death occurred amongst the previous twenty-five diabetic patients operated upon in this unit during the previous two and a half years, using earlier versions of the chart and achieving comparable accuracy of control.

The upper limit of 80 units/hour, which was set on the insulin infusion rate at the start of the study, may seem too high. As a result of our experience using the chart to control the blood glucose during intravenous feeding, we now use an upper limit of 20 units/hour. Even on those occasions, during the current study, when the insulin infusion rate was falling after a period at this very high insulin infusion rate, hypoglycaemia did not occur.

The method in each of its forms is simple, reliable, effective and safe. It is well liked by the nursing staff who prefer to use the computerised version. We suggest that it represents a major advance in the care of diabetic patients, for whom metabolic control is mandatory both at the time of major surgery and postoperatively, by making accurate control easy.

Acknowledgments

We thank the anaesthetists who allowed access to patients under their control, the technicians from the Medical Physics Department, particularly Paul Weatherston, and most of all, the nursing staff in the Cardiothoracic intensive care unit, who did most of the estimations.

References

1. ALBERTI KGMM, GILL GV, ELLIOTT MJ. Insulin delivery during surgery in the diabetic patient. *Diabetes Care* 1982; **5** (Supplement 1): 65–77.
2. ELLIOTT MJ, GILL GV, HOME PD, NOY GA, HOLDEN MP, ALBERTI KGMM. A comparison of two regimens for the management of diabetes during open-heart surgery. *Anesthesiology* 1984; **60**: 364–8.
3. MCKNIGHT CK, ELLIOTT MJ, PEARSON DT, HOLDEN MP, ALBERTI KGMM. Continuous blood glucose monitoring in open-heart surgery. *British Journal of Anaesthesia* 1985; **57**: 595–601.
4. WALFORD S, HOME PD, ALBERTI KGMM. A laboratory trial of two new blood glucose reflectance meters featuring automatic external calibration. *Annals of Clinical Biochemistry* 1984; **21**: 116–19.
5. KUNTSCHEN F, GALLETTI PM, HAHN C. Blood glucose control by closed loop insulin delivery during coronary artery bypass surgery. *Transactions of the American Society for Artificial Internal Organs* 1981; **27**: 241–5.
6. KUNTSCHEN FR, TAILLENS C, GALLETTI PM, HAUF E, HAHN C. Coronary surgery in diabetics: metabolic aspects of glycemia control by an artificial pancreas. *Transactions of the American Society for Artificial Internal Organs* 1982; **28**: 236–9.
7. BOWEN DJ, DAYKIN AP, NANCEKIEVILL ML, NORMAN J. Insulin-dependent diabetic patients during surgery and labour. *Anaesthesia* 1984; **39**: 407–11.
8. GILL GV, SHERIF IH, ALBERTI KGMM. Management of diabetes during open heart surgery. *British Journal of Surgery* 1981; **68**: 171–2.

Anaesthesia, 1986, Volume 41, pages 258–262

Anxiety levels in junior anaesthetists during early training

C. A. PINNOCK, A. E. ELLING, R. J. EASTLEY AND G. SMITH

Summary

Trait anxiety levels (predisposition to anxiety) and personality profiles were recorded in four novice anaesthetists prior to the start of their training in anaesthesia. State anxiety (the extent of anxiety at the moment of testing) was also assessed before and after the transition from accompanied to solo anaesthetic practice. There was no demonstrable difference in anxiety scores as a result of 'going solo' in any subject.

Key words

Anaesthesia; training.

It is generally held that the practice of anaesthesia is stressful and that working practice is accompanied by a degree of anxiety which varies according to the type of anaesthesia undertaken, the condition of the patient and the extent of surgery, as well as the personality of the individual practitioner.[1]

Training in anaesthesia in the majority of centres in the United Kingdom takes the form of an introductory period of approximately 3 months duration, during which the novice is not permitted to practise anaesthesia unless accompanied by a senior colleague. Thereafter, the trainee is allowed to practise, progressively unaccompanied, on relatively healthy patients undergoing surgery of increasing duration and complexity. It is reasonable to assume that the onset of solo practice is likely to be accompanied by an increase in the anxiety level of the novice. This hypothesis has been tested on four new trainee anaesthetists. They were examined over their introductory 3-month course and into 'flying solo' by the use of the S–R Inventory of General Trait Anxiousness (SRGTA),[2] Spielberger State Trait Anxiety Index (STAI)[3] and Multiple Affect Adjective Check List (MAACL).[4] Since it has been suggested that personality types having a high level of trait anxiety may respond with greater increases in state anxiety during stressful situations,[5] we have related state anxiety to trait anxiety for each individual.

Personality variables are known to play a major role in job performance and satisfaction. In order to relate the personality of the subjects to their anxiety levels, the Cattell 16 PF form A was applied to provide a personality factor profile for each volunteer.

Methods

Four male subjects aged 24–28 years volunteered to participate in the study. These four individuals represent the Anaesthetic Senior House Officer intake for Leicester in August 1984 and the

---

C.A. Pinnock, MB, BS, FFARCS, Lecturer, A.E. Elling, SRN, Research Sister, R.J. Eastley, MB, BS, FFARCS, Senior Registrar, G. Smith, BSc, MD, FFARCS, Professor, Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW.

0003–2409/86/030258 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

opportunity was taken to study these through their common training. The volunteers were not informed of the purpose of the study. Each of the assessments was supervised by one of the authors (CAP), who had no influence on the training that the volunteers received. All subjects were devoid of experience in anaesthesia and had entered the specialty from preregistration posts or unrelated disciplines. Assessment of the subjects was undertaken each Wednesday at 13.00 hours during the 3-month introductory course. On each occasion, the following tests were applied in random order: Spielberger State Trait Anxiety Index form X1 (for state anxiety) and Multiple Adjective Affect Check List (MAACL). On each of these test occasions, arterial pressure and heart rate were recorded using a Copal semi-automated sphygmomanometer system.

On the first test occasion, the SRGTA was also applied together with the Spielberger STAI-Form X2, to measure the *trait* anxiety of each individual. The Spielberger State Trait Anxiety Index[3] consists of two portions, designed to measure anxiety state and anxiety trait respectively. Anxiety trait is a measure of an individual's proneness to anxiety whereas anxiety state is a measure of the individual's anxiety level *at that particular time*. Each portion of the test comprises 20 descriptive statements which subjects have to endorse using a four-point scale. STAI measurement of both state and trait anxiety has been thoroughly validated and normal ranges for different populations have been published. Scoring was accomplished using the STAI manual[3] and higher numerical scores indicate increased anxiety in both trait and state measures.

The Multiple Affect Adjective Checklist[4] is a large adjective checklist which has been designed to record the level of three components of affect—anxiety, depression and hostility. Only the anxiety component was examined in this study. In this test, subjects have to select adjectives which they feel are applicable at that time. Scoring was accomplished in the recommended manner, whereby 'anxiety present' words score 1 if selected and 'anxiety absent' words score 1 if not selected. As the MAACL has 11 anxiety present and 10 anxiety absent words the maximum anxiety score is 21. Wassenaar[6] has listed the adjectives in each category and showed this test to be of use in the measurement of anxiety state in pre-operative patients. The S–R Inventory of General Trait Anxiety presents four situations: interpersonal (meeting new people), physical danger, ambiguous (in a new situation) and innocuous (daily routines). Each of these four posed situations has 15 associated statements which subjects must endorse on a 5 point scale. Thus, a measure of anxiety trait can be obtained from the total score and the four individual components of the total may be studied.

On commencing 'solo' on-call responsibilities, testing was carried out at 09.00 hr in the same location as used previously, at the onset of each 24-hour on-call period for immediate duties. This was continued for the first six on-call nights (the rota being 1 in 5). Subsequently, STAI X1 forms were completed for the following five on-call periods, in the anaesthetic room itself prior to inducing the first emergency case of the day.

On completion of the study the Cattell 16 Personality Factor Form A was completed by each subject.[7] This is a complex questionnaire which yields a score for each of sixteen personality factors. The scores obtained can be compared with normative data on various populations. The short form of the 16 PF (form C) has been applied to a sample of anaesthetists by Reeve.[8] The Cattell 16 PF test has been thoroughly documented internationally,[9] and shown to be of use in selection committees. Although Reeve[8] used the Cattell 16 PF form C on anaesthetists, the more comprehensive form A is designed for literate and more intelligent subjects, so it was decided that it would be more appropriate for use in this instance.

Results

Mean STAI and MAACL measurements were calculated for each individual over each of the three periods—'training' (accompanied practice), 'on-call' (prior to the start of an on-call day) and 'anaesthetic room' (prior to inducing anaesthesia) and compared with the training levels using the unpaired *t*-test (Table 1). No significant differences were found. Arterial pressure and heart rate data were compared using the unpaired *t*-test. There were no significant changes in these parameters in any individual over the study period.

On the test occasion during week seven of the introductory course, all subjects showed an increased STAI score accompanied by an increase in MAACL which was, however, not maintained into the following week. It was discovered that

Table 1. Mean anxiety scores for each subject over the three periods

	State Trait Anxiety Index (STAI)			Multiple Affect Adjecture Check list (MAACL)	
Subject	Training	On-call	Anaesthetic room	Training	On-call
A	44.5	41.8	41.8	8	9
B	39.0	36.0	40.0	7	7
C	33.0	32.0	32.0	7	6
D	35.0	38.6	35.8	7	8

Table 2. Trait anxiety scores of the subjects

	S-R Index of General Trait Anxiousness (SRGTA)				State Trait Anxiety Index (STAI)
Subject	Interpersonal	Danger	Ambiguous	Innocuous	
A	14	18	16	14	40
B	13	29	22	11	38
C	10	14	18	13	31
D	18	13	23	20	45
Normal adult male sample mean (SD)	22 (5.8)	31 (7.0)	25 (6.0)	19 (5.8)	38 (8.0)

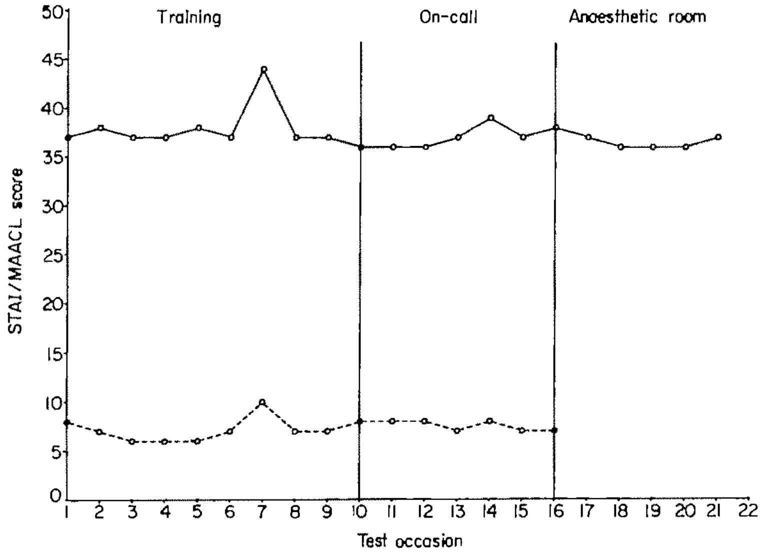


Fig. 1. Changes in state anxiety recorded by STAI and MAACL (mean scores) over the three periods: 'training' (accompanied practice), 'on-call' (prior to starting an on-call day) and 'anaesthetic room' (prior to inducing anaesthesia). ——, STAI; ——, MAACL.

prior to the test on week seven, a verbal disciplinary warning had been delivered to the subjects by the head of department. This appears to validate the accuracy of the tests in recording changes in state anxiety. However, as these results were not typical of a normal working day they were eliminated from the calculation of mean scores to avoid bias.

Discussion

Trait anxiety for three of the subjects was within one standard deviation of the reported mean for 'normal' adult males, as measured by STAI, but subject C had a lower than expected score (Table 2). Within the different categories of the SRGTA, subjects A, B and C had a low score for

Table 3. Factors in the 16 PF in which the four subjects were considered strongly deviant

Subject	Sten	Factor
A	10	B
	3	E
	10	F
	8	I
	8	Q1
B	3	A
	9	B
	8	E
	1	I
	2	N
	3	Q1
	8	Q3
C	10	B
	3	E
	10	F
	8	I
	8	M
	8	Q
D	3	A
	8	C
	10	E
	8	F
	8	L
	1	O
	3	Q3
	8	Q4

the interpersonal situation (that is to say outside of one standard deviation of the reported normal range), subjects A and C had a low score for the ambiguous situation but only subject B had a low score for the innocuous situation (daily routines) from which it might have been expected that this subject would show lesser changes in state anxiety than his colleagues. In fact, the magnitude of changes in state anxiety over the test periods was comparable in all four subjects. Subjects A, C and D exhibited low anxiety levels for the physical danger situation, C and D particularly so.

The previously described correlation between SRGTA Interpersonal Situation and STAI has been confirmed,[5] the rank order of trait anxiety for the subjects being the same in both these assessments. All subjects showed the same pattern of A-state response over the 16-week period (Fig. 1). No increase in state anxiety occurred on transition from accompanied practice to 'solo' (Table 1). It is interesting to note the sharp change in anxiety scores for both STAI and MAACL in week seven which was seen in all four subjects in response to the disciplinary interview, which indicates that both tests have sufficient sensitivity to record acute A-state changes. Subject C, whose A-trait was less than 'normal', showed no difference in A-state changes when compared with his colleagues. It would thus appear that the anticipation of anaesthetic practice is not an anxiety provoking event.

It was considered likely that A-state, if measured in the anaesthetic room prior to a demanding case, would be elevated above 'normal'. Accordingly, the study was continued for a further five on-call days. For simplicity, subjects filled in the STAI only in the anaesthetic room, immediately prior to inducing their first emergency case of the day. It is interesting to note that no increase in state anxiety occurred during this time and the scores for training, on-call and anaesthetic room were not significantly different, nor were there any changes in the more objective measurements of heart rate and arterial pressure.

The Cattell 16 PF scores are expressed as 'stens', that is on a scale of 1–10, after being corrected for a normal distribution. The raw scores were corrected by use of the normative data published from a large sample of British males.[10] Each factor in the 16 PF yields a sten between 1 and 10 and a value of 5.5 therefore corresponds to the population mean in the norm scales.[10] Stens of 5 or 6 are half a standard deviation below and above the mean, respectively while stens of 1 or 10 are two and a half standard deviations removed from the mean. The handbook to the 16 PF[9] states that stens of 4 or 7 on a factor are considered slightly deviant, whereas stens of 2/3 or 9/10 are strongly deviant. The factors in which the four subjects in this study showed strong deviance are listed in Table 3 (the 16 PF factors are listed in the appendix to this article).

A wide variation in personality profile was apparent between the subjects. Reeve[8] states that, in comparison to the general public, anaesthetists are less outgoing (factors A, H), brighter (B), more dominant (E), more serious (F), less sure (O), more self sufficient (Q2) and more tense (Q4). Table 3 demonstrates that this profile is not matched by each of these subjects. Using the 'stability index' proposed by Reeve (a cluster of factors C, F, O and Q4), all four subjects exceeded the minimum cumulative score of 16 and may thus be designated 'stable'. The O factor (confident–unsure) was considered to be most likely to correlate with trait anxiety and the rank order of subjects for this factor (subject D-sten 1, B-4, A-5, C-6) correlates well with the rank order of STAI trait anxiety scores.

It is concluded, therefore, that with subjects who fall within one standard deviation of their predicted trait anxiety, a 3-month introductory course of training permits the junior anaesthetist to practise independently, without undue anxiety. However, it would be interesting for those departments which utilise a shorter accompanied training period to determine if anxiety levels are augmented by the assumption of independent practice.

Acknowledgments

The Spielberger STAI Forms X1 and X2 are reproduced by special permission of the publisher, Consulting Psychologists Press Inc., Palo Alto, CA 943 06 from Self Evaluation Questionnaire (Form X)' by Spielberger C.D., Gorsuch R.L., Lushene R.E., Copyright 1968, 1977. Further reproduction is prohibited without the publisher's consent.

The Cattell 16 PF form A was reproduced by kind permission of the publisher, NFER Nelson Ltd, Darville House, Windsor, Berks SL4 1DF. Copyright 1957, 1961, 1962, 1967, 1979. Institute for Personality and Ability Testing, Champaign, Illinois, U.S.A. Further reproduction is prohibited without the publisher's consent.

References

1. Klein L. *The role of the anaesthetist—an exploratory study.* Basingstoke: Taylor and Francis, 1982.
2. Endler NS, Okada M. A multidimensional measure of trait anxiety: the S-R inventory of general trait anxiousness. *Journal of Consulting and Clinical Psychology* 1974; **43:** 319–29.
3. Spielberger CD, Gorsuch RE. *STAI manual for the state-trait anxiety inventory.* Palo Alto: Consulting Psychologists Press, 1970.
4. Zuckerman M, Lubin B, Vogel L, Valerius E. Measurement of experimentally induced affects. *Journal of Consulting Psychology* 1964; **28:** 418–25.
5. Kendall PC. Anxiety: states, traits—situations? *Journal Of Consulting and Clinical Psychology* 1978; **46:** 280–7.
6. Wassenaar W, Lancee WJ, Galloon S, Gale GD. The measurement of anxiety in the pre-surgical patient. *British Journal of Anaesthesia* 1977; **49:** 605–8.
7. Cattell RB, Saunders DR, Stice GP. The sixteen personality factor questionnaire. Champaign, Illinois: Institute for Personality and Ability Testing, 1950.
8. Reeve PE. Personality characteristics of a sample of anaesthetists. *Anaesthesia* 1980; **35:** 559–68.
9. Cattell RB, Eber HW, Tatsuoka M. *Handbook for the 16 PF questionnaire.* Champaign, Illinois: Institute for Personality and Ability Testing, 1970.
10. Saville P. *The British standardisation of the 16PF, supplement of norms, forms A and B.* Windsor: NFER Publishing Company Ltd., 1972.

Appendix

Descriptive statements of each factor of the 16 PF expressed as a continuum between two extremes.

(A) Reserved–Outgoing
(B) Less intelligent–More intelligent
(C) Affected by feelings–Emotionally stable
(E) Humble–Assertive
(F) Sober–Happy go lucky
(G) Expedient–Conscientious
(H) Shy–Venturesome
(I) Tough minded–Tender minded
(L) Trusting–Suspicious
(M) Practical–Imaginative
(N) Forthright–Shrewd
(O) Self assured–Apprehensive
(Q1) Conservative–Experimenting
(Q2) Group dependent–Self sufficient
(Q3) Undisciplined–Controlled
(Q4) Relaxed–Tense

Anaesthesia, 1986, Volume 41, pages 263–267

Meptazinol versus pethidine for postoperative pain relief in children

S. A. RIDLEY, N. C. MATTHEWS AND J. DIXON

Summary

A double-blind, randomised, clinical trial was undertaken comparing intramuscular meptazinol (1 mg/kg) with intramuscular pethidine (1 mg/kg) for the relief of post-tonsillectomy pain, in 100 children under 15 years of age. Pethidine provided better analgesia in those patients who were awake after 30 minutes, but thereafter no statistically significant differences between the degree of pain relief could be detected. Meptazinol caused less sedation than pethidine, in that significantly more patients were awake after 40 minutes in the meptazinol group. The incidence of nausea and vomiting was similar in patients of both groups.

Key words

Pain; postoperative.
Analgesics, narcotic; pethidine, meptazinol.

Meptazinol is a potent, centrally-acting analgesic with opioid antagonist properties. However, certain features of its pharmacology, such as a low incidence of respiratory depression[1] and an equi-analgesic efficiency of the dextro- and laevo-isomers, are atypical of the commonly used opioids. In adults, meptazinol has been shown to be equi-analgesic with pethidine following abdominal and orthopaedic operations.[2] The relative lack of respiratory depression as compared with pethidine is an obvious advantage.

Meptazinol has not been studied as an analgesic in children, and hence we decided to compare its analgesic efficacy with that of pethidine in children undergoing tonsillectomy.

Methods

One hundred children in whom tonsillectomy alone, or combined with adenoidectomy or insertion of grommets, were studied. Informed parental consent was obtained and the study was approved by the hospital Ethical Committee. All patients were aged less than 15 years old and medically fit.

The children were premedicated with trimeprazine 3 mg/kg, up to a maximum dose of 120 mg, 2 hours prior to the induction of anaesthesia. On arrival in the anaesthetic room, anaesthesia was induced with thiopentone 5 mg/kg and tracheal intubation was facilitated by suxamethonium 2 mg/kg. Anaesthesia was maintained with halothane (1–3%) and 33% oxygen in nitrous oxide. Any other drugs, such as atropine, were given at the discretion of the anaesthetist and noted. At the end of surgery, the inhalational agents were discontinued and the patient's trachea extubated. An intramuscular injection

---

S.A. Ridley, MB, BS, FFARCS, Registrar, N.C. Matthews, MB, ChB, Registrar, J. Dixon, MB, BS, FFARCS, Senior Registrar, Royal Devon and Exeter Hospital (Wonford), Barrack Road, Exeter EX2 5DW.

0003–2409/86/030263 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

in the lateral compartment of the thigh of either meptazinol or pethidine (1 mg/kg in both cases) was then given in a double-blind, randomised fashion, such that 50 patients received each drug.

During recovery, the following times from the injection of analgesic drug to each event were recorded: time to protrude airway, time to stir (defined as an obvious purposeful movement), time to vocalise, either words or groan. At 30, 60, 120 and 240 minutes after the injection of analgesic drug a note was made of pulse rate, respiratory rate, objective assessment of the child's pain using a 10-cm linear analogue scale (ranging from no pain, 0, to severe pain, 10) and a five point verbal scale (Table 1).

Patients were seen on the first postoperative day and an assessment of the overall efficiency of the pain relief achieved was made and graded as follows: excellent if only one injection of analgesic was given, the patient was eating normally and denied that the throat had been painful; satisfactory, as above, except that the child complained the sore throat was for them as bad as an attack of tonsillitis; poor, if a further injection of analgesic was required or the child had been distressed and admitted that the pain was worse than any previous tonsillitis.

The observations were made by one of the investigators, either in the recovery area or later on the main ward. If the initial dose of analgesic provided inadequate pain relief, then a further injection of pethidine (1 mg/kg) was given intramuscularly.

The results were analysed with the appropriate Student's *t*-test, Chi squared test and Wilcoxon's rank sum test.

Table 1. Grading system for objective pain assessment

Grade	Description of patient
1	Asleep
2	Awake and calm
3	Awake and agitated
4	Crying intermittently
5	Crying continuously

Results

There were no significant differences between the groups with regard to age, weight, time of premedication prior to surgery, duration or type of operation. (Table 2).

Recovery from anaesthesia as judged by the time of stirring positively, protruding airway and vocalising is shown in the cumulative frequency graphs in Figs 1–3. In both groups, 70% of the patients had recovered in one hour, but at 40 minutes significantly more of the meptazinol group were awake ($p<0.05$). Table 3 shows the mean of pulse and respiratory rates at 30, 60, 120 and 240 minutes after the injection of analgesic. There is no significant difference between the two groups with regard to these two measurements.

The degree of analgesia provided, as recorded on the visual analogue scale, is shown in Fig. 4. In those patients who were awake, the visual analogue scales have been grouped and displayed as histograms. There was no significant difference between the degree of analgesia at any time between the groups, except at the initial 30 minute assessment, where the patients who had received pethidine had lower scores (better analgesia) than those who received meptazinol. Comparison between the objective assessment of pain using the five point verbal scale did not detect any significant difference between the groups at any time (Table 4).

Table 2. Patients' age, weight, time of premedication, duration of surgery and procedure in both groups (mean, SD)

	Pethidine	Meptazinol
Age (years)	9.0 (3.8)	8.2 (3.3)
Weight (kg)	34.7 (14.6)	31.6 (15.4)
Time of premedication (in minutes before induction)	122 (19.9)	122 (23.7)
Duration of operation (minutes)	25.7 (8.7)	24.5 (7.6)
Type of operation		
Tonsillectomy alone	23	16
Adenotonsillectomy	15	25
Adenotonsillectomy and insertion of grommets	12	9

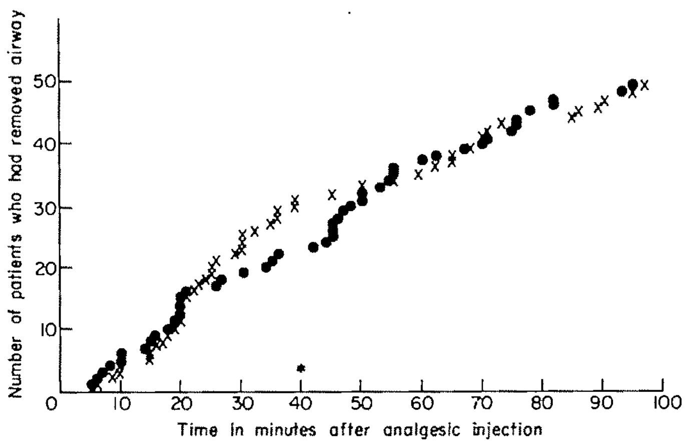


Fig. 1. Cumulative frequency showing the number of patients who had stirred positively against time in minutes after analgesic injection. ●, Pethidine group; meptazinol group.

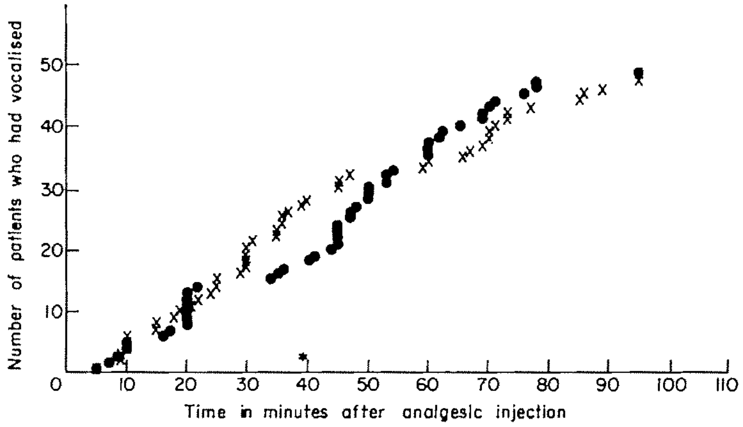


Fig. 2. Cumulative frequency showing the number of patients who had protruded their airway against time in minutes after analgesic injection. ●, Pethidine group; meptazinol group; *, $p<0.05$.

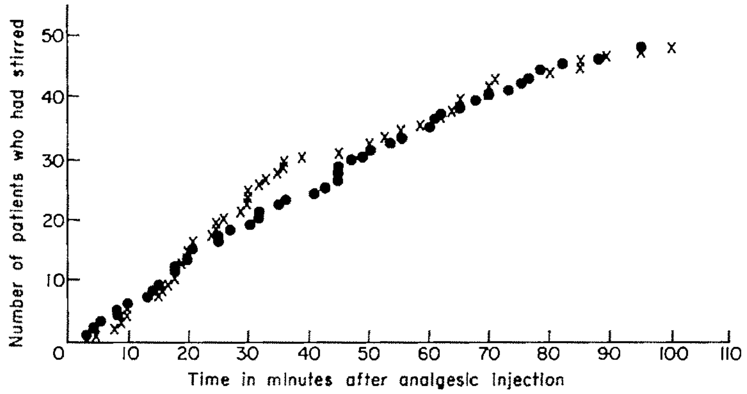


Fig. 3. Cumulative frequency showing the number of patients who had vocalised against time in minutes after analgesic injection. ●, Pethidine group; ×, meptazinol group; *, $p<0.05$.

Table 3. Respiratory rate (mean, SD) varying with time after analgesic injection

	Time after injection (minutes)			
	30	60	120	240
Pethidine	19.0 (3.9)	19.3 (4.1)	18.4 (4.3)	18.8 (3.9)
Meptazinol	18.9 (3.5)	18.5 (3.5)	18.6 (3.1)	19.3 (2.8)

Heart rate (mean, SD) varying with time after analgesic injection

	Time after injection (minutes)			
	30	60	120	240
Pethidine	107 (19)	103 (17)	103 (20)	107 (19)
Meptazinol	109 (15)	105 (18)	104 (17)	107 (14)

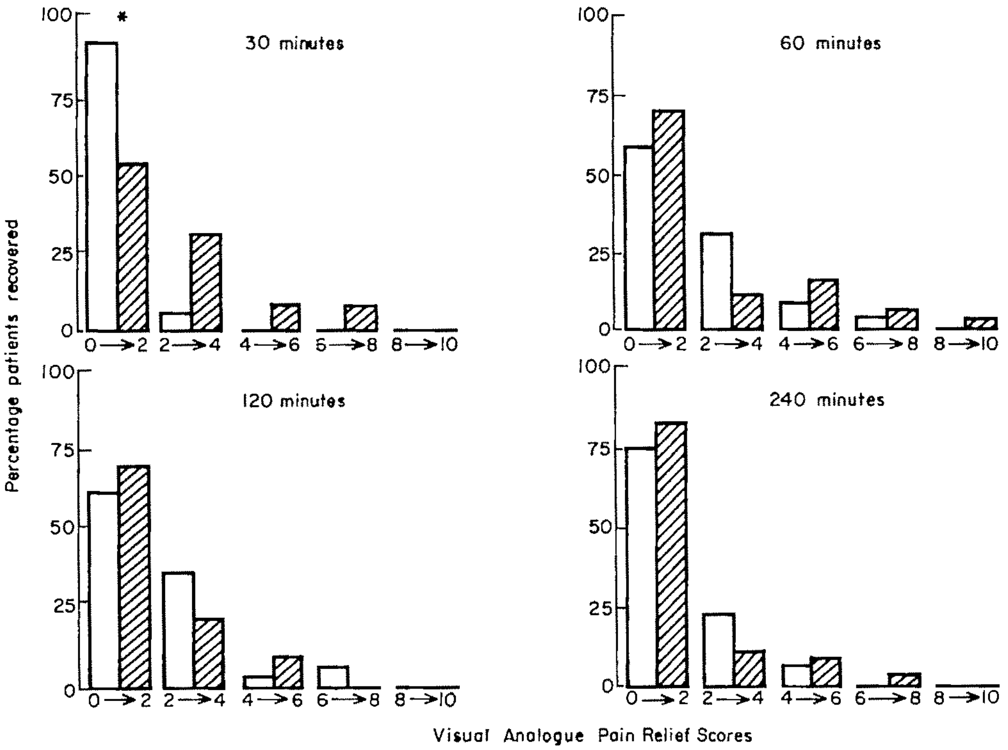


Fig. 4. Histograms showing the visual analogue pain relief scores of those patients who had recovered from anaesthesia at 30, 60, 120 and 240 minutes after analgesic injection. □, Pethidine group; ■, meptazinol group; *, $p<0.05$.

At the follow-up visit the next day, there was no significant difference between the efficacy of the overall level of analgesia provided (Table 5), the incidence of nausea/vomiting and additional pain relief required (Table 6). Nineteen patients were lost to follow-up.

Discussion

Pethidine provided better analgesia in those patients who recovered quickly after anaesthesia when assessed by means of the visual analogue scale. This may be a reflection of the

Table 4. Distribution of objective assessment grades of patients in both groups varying with time after analgesic injection. Pethidine group (P); meptazinol group (M)

	Time after analgesic injection (minutes)							
	30		60		120		240	
Grade	P	M	P	M	P	M	P	M
1	10	8	18	21	36	37	39	35
2	5	8	16	9	8	8	8	10
3	1	3	2	3	2	2	2	0
4	2	7	1	6	4	3	1	4
5	0	0	0	0	0	0	0	1
No. of patients awake	18	26	37	39	50	50	50	50

Table 5. The distribution of assessment of overall efficacy of pain relief between pethidine and meptazinol

	Degree of pain relief		
Group	Excellent	Satisfactory	Poor
Pethidine	7	30	4
Meptazinol	4	28	8

19 patients were lost to follow up.

Table 6. Incidence of side effects in the two groups

Group	Nausea/vomiting	Inadequate analgesia
Pethidine	3	2
Meptazinol	4	3

different pharmacokinetic properties of the two drugs, in that intramuscular pethidine has an onset of action within 10 minutes,[3] while that of meptazinol is slightly longer.[4] Both agents, when given intramuscularly, have a peak effect at one hour and subsequent assessments with both the objective pain scale and visual analogue scale show meptazinol and pethidine to be equally effective. The fact that a difference in analgesia was detected on the visual analogue scale but not the objective pain scale may reflect the greater sensitivity of the former as a means of assessment.

The similarity in analgesic efficiency is also demonstrated by the lack of difference between the respiratory and pulse rates in the two groups, if these two measurements are used as objective data in the assessment of pain relief. Simple recording of the respiratory rate is not sufficiently sensitive to show any minor changes in respiratory function due to drug induced respiratory depression. Therefore, no conclusion regarding respiratory function in these children could be made, except that profound respiratory depression was not seen in either group.

A previous study in adults showed that meptazinol caused less sedation than pethidine, 2% compared with 8%,[5] and the significantly greater number of patients awake in the meptazinol group at 40 minutes could support this. However, the incidence of nausea and vomiting after the two drugs was similar and our results support this.

We conclude that, allowing for the longer onset of action of meptazinol, pethidine and meptazinol in the dosage used are equally effective in providing pain relief for this type of surgery in children. However, the faster initial recovery and consequent return of the protective reflexes in patients who received meptazinol is a positive advantage after surgery on the upper airway. This may make meptazinol a more suitable drug.

Acknowledgments

The authors wish to thank Wyeth Laboratories for supplying all the analgesics used, and Mrs A. Foster for her secretarial assistance.

References

1. Jordan C, Lehane JR, Robson PJ, James JG. A comparison of respiratory effects of meptazinol, pentazocine and morphine. *British Journal of Anaesthesia* 1979; **51**: 497–502.
2. Paymaster NJ. Intramuscular meptazinol analgesia after surgery: a study of the dose-response effect and a controlled comparison with pentazocine and pethidine. *Postgraduate Medical Journal* 1983; **59** (suppl 1): 25–31.
3. Goodman L, Gilman A. *The pharmacological basis of therapeutics* 6th edn. London: Baillière-Tindall, 1980.
4. Stephens RJ, Waterfall JF, Franklin RA. A review of the biological properties and metabolic disposition of the new analgesic agent, meptazinol. *General Pharmacology* 1978; **9**: 73–8.
5. Nicholas ADG, Robson PJ. Double-blind comparison of meptazinol and pethidine in labour. *British Journal of Obstetrics and Gynaecology* 1982; **89**: 318–22.

Anaesthesia, 1986, Volume 41, pages 268–271

Influence of induction of anaesthesia with midazolam on the neuro-endocrine response to surgery

D. DAWSON AND J. W. SEAR

Summary

The effect of midazolam, for induction of anaesthesia, on the glycaemic and adrenocortical responses to lower pelvic surgery in female patients has been studied and compared with a comparable group of patients receiving thiopentone. Although midazolam has been shown to obtund adrenaline and noradrenaline release to electrical or surgical stress in the rat and dog, there was no blunting of the glycaemic response to surgery in man. Plasma cortisol levels in response to surgery and anaesthesia were comparable in the two groups of patients.

Key words

Metabolism; glucose.
Hormones; corticosteroid.

Among recent methods investigated for the attenuation of the stress response to surgery and trauma is the use of endocrine manipulation (by infusions of insulin, or the administration of etomidate) to inhibit the release of catabolic hormones.[1-3] The increased levels of catecholamines seen following surgical stress have been implicated as the cause of the hyperglycaemic response to surgery, through a failure of insulin secretion.[4,5] In the rat, the water soluble benzodiazepine midazolam diminishes the adrenal response to electrical stress, probably as a consequence of the drug's centrally mediated anxiolytic action.[6] If midazolam were shown to suppress the adrenal cortex and/or medulla responses in man, it might provide a beneficial effect to the surgical patient.

There are, however, no reported data on the influence of midazolam as an induction agent upon the neuro-endocrine response to surgery. This study describes a comparison with thiopentone in twelve premenopausal women undergoing abdominal hysterectomy.

Methods

Twelve women scheduled to undergo total abdominal hysterectomy were studied after they had given their informed consent to the sampling of blood. Ethical approval for the study was obtained from the local Hospital Ethics Committee. No patient had any serious medical disorder, and none were receiving any intercurrent medication or were clinically postmenopausal. All patients had values in the normal range for pre-operative haematology and biochemistry analyses. Patients studied were either first or second on a morning operating list to avoid any

---

D. Dawson, MB, ChB, FFARCS, Senior Registrar, J. W. Sear, BSc, PhD, FFARCS, Clinical Reader and Hon Consultant, Nuffield Department of Anaesthetics, John Radcliffe Hospital, Headington, Oxford OX3 9DU.
Correspondence should be addressed to Dr J.W. Sear please.

0003–2403/86/030268 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

influence of the normal diurnal variation of hormone concentrations.

Following premedication with oral diazepam 10 mg 2 hours before surgery, anaesthesia was induced with thiopentone 4–5 mg/kg or midazolam 20 mg, and then maintained with 67% nitrous oxide in oxygen supplemented by 0.2% inspired concentration of enflurane. Analgesia was provided by fentanyl 3 μg/kg and neuromuscular blockade by alcuronium 0.25 mg/kg. Patients' lungs were ventilated using a Bain system, with a fresh gas flow of 70 ml/kg/minute and a tidal volume of 10 ml/kg. Allocation to receive thiopentone or midazolam was on a random basis.

Intra-operatively, the electrocardiogram and heart rate were monitored continuously, and blood pressure measured by the Dinamap automatic recorder. Fluid administration was with Hartmann's solution, 5 ml/kg/hour. No patient required blood. At the end of surgery, residual neuromuscular blockade was reversed with intravenous atropine 1.2 mg and neostigmine 2.5 mg. Postoperative analgesia was provided by intramuscular papaveretum 10–15 mg.

Table 1. Patient and anaesthesia data. Mean values (SEM). Six patients in each group

	Midazolam	Thiopentone
Age (years)	39.8 (3.9)	41.2 (1.2)
Weight (kg)	62.9 (5.2)	61.5 (3.9)
Time from premed. to induction (minutes)	114.7 (4.7)	109.2 (9.6)
Duration of anaesthesia (minutes)	90.7 (15.2)	79.8 (7.8)
Duration of surgery (minutes)	73.3 (12.9)	64.5 (7.3)

Blood sampling

Blood was collected without use of a tourniquet before induction of anaesthesia (sample 1), at the end of surgery (sample 2), at 4 hours (sample 3), at 10 hours (sample 4), and at 24 hours (sample 5) after induction of anaesthesia. Samples were taken from a peripheral venous cannula and collected into tubes containing lithium heparin and fluoride-oxalate anticoagulants. The samples were immediately placed in melting ice, centrifuged within 2 hours of collection, and the plasma was separated and stored frozen. Plasma glucose was measured using a Beckman glucose analyser (based on the glucose oxidase reaction) and cortisol by a standard radio-immunoassay (Bioanalysis, Cardiff, Wales).

Statistical analysis was by the Wilcoxon matched pairs signed ranks test for a change within a group with respect to time; the Mann–Whitney U test was used for differences between groups with time. Data are shown as mean and standard error of the mean (SEM) unless otherwise stated.

Results

There were no significant differences between the two groups ($n = 6$ in each group) for age, weight, time from premedication to induction of anaes-

Table 2. Plasma glucose (mmol/litre) and plasma cortisol (nmol/litre) levels in the two groups of patients receiving either midazolam or thiopentone for induction of anaesthesia. Mean values (SEM). Comparison within groups by Wilcoxon matched pairs signed ranks test, and between groups by the Whitney Mann U test.

	Midazolam	Thiopentone	Significance Midazolam vs thiopentone
Glucose			
S1 (pre-induction)	4.68 (0.12)	4.53 (0.27)	NS
S2 (at end of surgery)	6.57 (0.34)**	6.02 (0.43)**	NS
S3 (at four hours)	7.42 (0.66)**	7.48 (1.14)**	NS
S4 (at ten hours)	8.78 (0.19)**	9.85 (1.39)**	NS
S5 (at twenty four hours)	6.62 (0.35)**	5.73 (0.53)**	NS
Cortisol			
S1	461 (82)	303 (52)	NS
S2	880 (78)**	852 (46)**	NS
S3	1178 (81)**	1098 (81)**	NS
S4	1024 (63)**	953 (119)**	NS
S5	754 (109)	459 (84)	$p = 0.032$

**, $p < 0.01$; NS, not significant.

thesia, or duration of anaesthesia or surgery (Table 1). Anaesthesia was induced in all patients between 08.00 and 09.30 hours; the thiopentone group received a mean dose of thiopentone of 259 mg (SEM 8 mg). Anaesthesia was clinically uneventful in all patients.

Hormone and glucose concentrations are shown in Table 2. Plasma cortisol concentrations rose in both groups, and were significantly greater than at induction of anaesthesia in samples 2–4 ($p < 0.01$). The cortisol levels at 24 hours were not significantly different from pre-induction values in either group, although the concentration in the midazolam group was significantly greater than that in the thiopentone group ($p = 0.032$).

Plasma glucose concentrations rose significantly during and after operation in both groups of patients. There was no difference between groups at any sample time, and the glycaemic response to surgery persisted for up to 24 hours.

Discussion

Why should we want to develop anaesthetic techniques that suppress the normal neuro-endocrine response to surgery? Kehlet[7] has shown that if the glycoregulatory responses are obtunded, an improved postoperative nitrogen balance may result. Several techniques have been successfully employed to block the peri-operative increases in adrenal steroid secretion. These include extensive extradural anaesthesia,[8] large doses of opioids,[9-11] extradural morphine or diamorphine[12,13] and intrathecal morphine.[14] In addition, etomidate by infusion will obtund the response for up to 24 hours,[15] but this latter technique is accompanied by a failure of adrenocorticotrophic hormone (ACTH) to increase the plasma concentration of either cortisol or aldosterone significantly.[16]

Sympathetic stimulation during surgery results in increased glycogenolysis, lipolysis and gluconeogenesis. In addition, there is evidence that adrenergic receptor activity may also influence ACTH and cortisol release.[17] Reduction of the glycaemic response requires blockade of both α_1 and β receptors; studies have shown the hyperglycaemia to be abolished by extradural analgesia,[18] and α adrenergic blockade,[19] and the onset to be delayed by labetalol.[20]

Midazolam, a water soluble benzodiazepine has been shown in man to reduce pre-induction antidiuretic hormone levels when used as overnight pre-operative sedation.[2] In the dog, midazolam obtunded the increase in adrenaline and noradrenaline in response to the stimulus of surgery.[22] However, despite the postulate of Glisson and his colleagues that midazolam in subanaesthetic doses inhibits catecholamine release through a central GABA interaction,[22] our study shows that the glycaemic response to surgery is not obtunded in man. If midazolam does reduce catecholamine release in man, stress hyperglycaemia may still result from direct stimulation of sympathetic nerves to the liver.

That midazolam has no effect on the adrenocortical response to surgery is not surprising. Engquist *et al.*[8] have shown the cortisol response to surgery to occur unless both afferent somatic and autonomic pathways are blocked. However, Niv *et al.*[22] showed intrathecal midazolam to have an antinociceptive effect when supramaximal electrical stimulation is applied to the tibial nerve of the dog and the evoked responses are recorded in the renal sympathetic nerves. This may be the result of a local effect at the site of the intrathecal injection on GABA activity.

Thus, use of intravenous midazolam for the induction of anaesthesia in ill surgical patients would appear to be an alternative agent to thiopentone from a haemodynamic point of view[23,24] and without the suppressive effects on adrenosteroidogenesis seen with etomidate.[25] Whether any reduction in the glycaemic response will occur with larger intravenous doses or an infusion of midazolam is not known, nor whether the effect of any reduction is too short lived to be detected by the present sampling regimen.

References

1. Hall GM, Walsh ES, Paterson JL, Mashiter K. Low-dose insulin infusion and substrate mobilization during surgery. *British Journal of Anaesthesia* 1983; **55:** 939–45.
2. Fragen RJ, Shanks CA, Molteni A, Avram MJ. Effects of etomidate on hormonal responses to surgical stress. *Anesthesiology* 1984; **61:** 652–6.
3. Fry DE, Griffiths H. The inhibition by etomidate of the 11 beta-hydroxylation of cortisol. *Clinical Endocrinology* 1984; **20:** 625–9.
4. deFronzo RA, Sherwin RS, Felig P. Synergistic interactions of counterregulatory hormones: a mechanism for stress hyperglycemia. *Acta Chirurgica Scandinavica* 1980; supplementum **498:** 33–42.

5. Allison SP. Changes in insulin secretion during open heart surgery. *British Journal of Anaesthesia* 1971; **43:** 138–43.
6. Prada M da, Pieri L, Picotti GB. Effects of midazolam (a water soluble benzodiazepine) on stress-induced increase of plasma catecholamines. In *Catecholamines and stress: recent advances* Osain, Kvetriansky and Kopin, eds. North Holland: Elsevier 1980; 231–6.
7. Kehlet H, Brandt MR, Prange Hansen A, Alberti KGMM. Effect of epidural analgesia on metabolic profiles during and after surgery. *British Journal of Surgery* 1979; **66:** 543–6.
8. Engquist A, Brandt MR, Fernandes A, Kehlet H. The blocking effect of epidural analgesia on the adrenocortical and hyperglycemic responses to surgery. *Acta Anaesthesiologica Scandinavica* 1977; **21:** 330–5.
9. George JM, Reier CE, Lanese RR, Rower JM. Morphine anesthesia blocks cortisol and growth hormone response to surgical stress in humans. *Journal of Clinical Endocrinology and Metabolism* 1974; **38:** 736–41.
10. Hall GM, Young C, Holdcroft A, Alaghband-Zadeh J. Substrate mobilization during surgery. A comparison between halothane and fentanyl anaesthesia. *Anaesthesia* 1978; **33:** 924–30.
11. Bovill JG, Sebel PS, Fiolet JWT, Touber JL, Kok K, Philbin DM. The influence of sufentanil on endocrine and metabolic responses to cardiac surgery. *Anesthesia and Analgesia* 1983; **62:** 391–7.
12. Christensen P, Brandt MR, Rem J, Kehlet H. Influence of extradural morphine on the adrenocortical and hyperglycaemic response to surgery. *British Journal of Anaesthesia* 1982; **54:** 23–6.
13. Cowen MJ, Bullingham RES, Paterson GMC, McQuay HJ, Turner M, Allen MC, Moore A. A controlled comparison of the effects of extradural diamorphine and bupivacaine on plasma glucose and plasma cortisol in postoperative patients. *Anesthesia and Analgesia* 1982; **61:** 15–8.
14. Moore RA, Paterson GMC, Bullingham RES, Allen MC, Baldwin D, McQuay HJ. Controlled comparison of intrathecal cinchocaine with intrathecal cinchocaine and morphine: clinical effects and plasma morphine concentrations. *British Journal of Anaesthesia* 1984; **56:** 837–41.
15. Moore RA, Allen MC, Wood PJ, Rees LH, Sear JW. Peri-operative endocrine effects of etomidate. *Anaesthesia* 1985; **40:** 124–30.
16. Wagner RL, White PF. Etomidate inhibits adrenocortical function in surgical patients. *Anesthesiology* 1984; **61:** 647–51.
17. Grossman A, Besser GM. Opiates control ACTH through a noradrenergic mechanism. *Clinical Endocrinology* 1982; **17:** 287–90.
18. Traynor C, Paterson JL, Ward ID, Morgan M, Hall GM. Effects of extradural analgesia and vagal blockade on the metabolic and endocrine response to upper abdominal surgery. *British Journal of Anaesthesia* 1982; **54:** 319–23.
19. Walsh ES, Paterson JL, Mashiter K, Hall GM. Effect of phentolamine on the metabolic response to gynaecological surgery. *British Journal of Anaesthesia* 1982; **54:** 517–21.
20. Child CS. The effect of labetalol on the cardiovascular, hyperglycaemic and adrenocortical responses to surgery. *Anaesthesia* 1984; **39:** 1192–6.
21. Sjövall S, Kanto J, Grönroos M, Himberg J-J, Kangas L, Viinamäki O. Antidiuretic hormone concentrations following midazolam premedication. *Anaesthesia* 1983; **38:** 1217–20.
22. Glisson SN, Haddad W, Kubak MA, Hieber MF. Midazolam action on catecholamine, cortisol and renin responses to surgical stress in dogs. *Anesthesiology* 1983; **59:** A239.
23. Niv D, Whitwam JG, Loh L. Depression of nociceptive sympathetic reflexes by the intrathecal administration of midazolam. *British Journal of Anaesthesia* 1983; **55:** 541–7.
24. Lebowitz PW, Cote ME, Daniels AL, Martyn JAJ, Teplick RS, Davison JK, Sunder N. Cardiovascular effects of midazolam and thiopentone for induction of anaesthesia in ill surgical patients. *Canadian Anaesthetists' Society Journal* 1983; **30:** 19–23.
25. Sear JW, Atherden S, Edwards CRW. Suppression of adrenal steroidogenesis in man by etomidate. *Journal of Endocrinology* 1985; **104:** (suppl) 90.

Anaesthesia, 1986, Volume 41, pages 272–275

Blood glucose in anaesthetised children

Comparison of blood glucose concentrations in children fasted for morning and afternoon surgery

NANCY REDFERN, G. M. ADDISON AND G. MEAKIN

Summary

Blood glucose levels were measured immediately after induction of anaesthesia and again intra-operatively in 26 children fasted overnight for operations in the morning and 28 children fasted from 8.00 a.m. for afternoon surgery. The mean post-induction glucose concentration of the afternoon surgery group was significantly lower than that of the morning group. However, no child in either group was hypoglycaemic. Anaesthesia and surgery caused significant increases in blood glucose levels. It is concluded that pre-operative fasting is well tolerated in healthy pre-school children, regardless of the timing of surgery.

Key words

Anaesthesia; paediatric.
Complications; hypoglycaemia.

Studies of the effects of pre-operative starvation on blood glucose levels in children have produced apparently conflicting results. Thomas[1] found that five out of 18 surgical inpatients aged less than 4 years were hypoglycaemic after fasting for 8–10 hours from 06.00 hours. However, in a subsequent study at the same institution, Graham[2] was unable to demonstrate hypoglycaemia in any of 31 surgical outpatients aged less than 5 years who were fasted overnight. This led to suggestions that perhaps inpatients differed from outpatients with regard to glucose homeostasis, or that an overnight fast might be better tolerated than one undertaken during the day.

The first of these hypotheses was examined by Jensen *et al.*,[3] who compared pre-operative glucose concentrations in children aged between 6 months and 9 years undergoing inpatient and outpatient surgery in the morning. These authors found no difference in pre-operative blood glucose concentrations between inpatients and outpatients, and only one case of hypoglycaemia in 92 patients fasted overnight.

The purpose of the present study was to determine whether children operated on in the afternoon were at greater risk of developing hypoglycaemia than those operated on in the morning.

Methods

Two groups of healthy children aged between 1 and 5 years, undergoing elective minor surgery were studied. The protocol for the study was approved by the Hospital Ethics Committee and

---

Nancy Redfern, BSc, FFARCS, Registrar in Anaesthetics,* G.M. Addison, PhD, MB, BChir, Consultant Chemical Pathologist, G. Meakin, MB, ChB, FFARCS, Consultant Paediatric Anaesthetist, Royal Manchester Children's Hospital, Pendlebury, Manchester M27 1HA.
*Present address: Department of Anaesthesia, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP.

0003–2409/86/030272 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

verbal consent was obtained from a parent. Twenty-six children were fasted overnight for operations in the morning (morning group), and 28 children were given a breakfast of cereal and milk and then fasted from 08.00 hours for afternoon surgery (afternoon group). Information was collected about the time and nature of the last food or drink and the childrens' weights were recorded.

Patients received either no premedication, trimeprazine 3 mg/kg orally 2 hours before operation, or temazepam 1 mg/kg orally 1 hour before operation. Anaesthesia was induced with thiopentone 4–8 mg/kg, followed by suxamethonium 1–2 mg/kg and atropine 15 μg/kg. Tracheal intubation was carried out and anaesthesia maintained with nitrous oxide, oxygen and halothane. Six children, three in the morning group and three in the afternoon group, who required anaesthesia for more than 45 minutes, received a long acting muscle relaxant and their lungs were ventilated.

Two samples of venous blood were withdrawn for glucose estimations, the first immediately after induction of anaesthesia (post-induction glucose) and the second 20 minutes later, a variable time after the commencement of surgery (intra-operative glucose). Samples were collected into fluoride bottles and analysed within 3 hours by a modification of the glucose oxidase/peroxidase method.[4] Hypoglycaemia was defined as a blood glucose concentration of less than 2.2 mmol/litre.[5]

Statistical differences were determined using Student's *t*-test. The null hypothesis was rejected when $p < 0.05$.

Results

The ages and weights of children in the morning and afternoon groups were comparable (Table 1). However, the mean fasting time of patients operated on in the morning was significantly longer than that of patients operated on in the afternoon ($p < 0.001$) (Table 2).

The blood glucose concentrations of both groups following induction of anaesthesia and during surgery are shown in Table 3. It is apparent that the mean post-induction glucose concentration of the afternoon group was slightly lower than that of the morning group, despite the shorter fasting period ($p < 0.05$). There was no correlation between the post-induction blood glucose level in individual cases, and the duration of fasting, which ranged from 6–21 hours. The mean intra-operative glucose concentrations of both groups were greater than their corresponding pre-operative values ($p < 0.001$), but the difference between them was not statistically significant. No child in the present study was hypoglycaemic; the lowest blood glucose observed was 2.6 mmol/litre.

Table 4 compares the blood glucose at induction of anaesthesia of unpremedicated patients and patients who received trimeprazine or temazepam. There was a trend towards higher blood glucose concentrations in premedicated patients compared to unpremedicated patients, and in patients premedicated with temazepam compared to trimeprazine. In patients operated on in the afternoon, the difference in blood glucose concentration between those premedicated with temazepam and those who received no premedication was statistically significant ($p < 0.05$).

Discussion

In the present study, the mean blood glucose following induction of anaesthesia was significantly lower in children operated on in the afternoon than in children fasted overnight for operation in the morning. However, the actual difference was small and none of our patients was hypoglycaemic.

The small diurnal variation in fasting blood glucose in our paediatric patients was similar to that found by Whichelow *et al.* in normal adult volunteers.[6] The cause for this variation remains uncertain, but it seems unlikely to be due to variations in the level of circulating insulin. Whichelow *et al.*[6] found no difference

Table 1. Population data

		Morning group	Afternoon group
Number of children		26	28
Age (years)	Mean	3.42	3.42
	SEM	0.18	0.21
	Range	1.08–4.91	1.16–4.91
Weight (kg)	Mean	16.0	15.7
	SEM	0.7	0.6
	Range	10.2–25.0	8.0–20.5

There were no statistically significant differences in mean ages or weights between the groups.

Table 2. Length of fast

		Morning group	Afternoon group	Significance
Length of fast (hours)	Mean	14.9	8.8	$p < 0.001$
	SEM	0.46	0.6	
	Range	9.4–18.8	6.7–20.6	

Table 3. Blood glucose concentrations during anaesthesia

		Morning group	Afternoon group	Significance
Post-induction blood glucose (mmol/litre)	Mean	4.8	4.4	$p < 0.05$*
	SEM	0.12	0.13	
	Range	3.0–6.5	3.1–6.1	
Intra-operative blood glucose (mmol/litre)	Mean	5.8	5.4	$p < 0.3$ ns*
	SEM	0.25	0.21	
	Range	3.4–8.7	2.6–7.3	
Significance		$p < 0.001$†	$p < 0.001$†	

* Comparison of morning and afternoon groups; † comparison of post-induction and intra-operative blood glucose concentrations.

Table 4. Blood glucose at induction of anaesthesia with different premedications

		No premedication	Trimeprazine	Temazepam
Morning group				
Number		13	6	7
Blood glucose (mmol/litre)	Mean	4.6	4.7	5.1
	SEM	0.18	0.14	0.26
Afternoon group				
Number		7	16	5
Blood glucose (mmol/litre)	Mean	4.1	4.4	4.8*
	SEM	0.14	0.20	0.25

* $p < 0.05$ compared with unpremedicated patients.

in the fasting morning and afternoon insulin levels, and insulin levels after intravenous glucose were lower in the afternoon than in the morning. Moreover, there is evidence of increased resistance to the peripheral effects of insulin in the afternoon.[7]

Diurnal variation in the level of circulating cortisol provides a possible explanation for higher blood glucose levels in the morning. The plasma concentration of this hormone is higher in the morning than in the afternoon, and it produces a hyperglycaemic effect by increasing the activity of hepatic glucose-6-phosphatase, and possibly by slowing intracellular phosphorylation of glucose.[8]

The increase in mean blood glucose following the onset of surgery was approximately 1 mmol/litre in both morning and afternoon groups, which was similar to that previously reported in children.[9] Individual responses were variable and, in nine of our children, intra-operative glucose levels were lower than the values after induction.

The trend towards higher blood glucose concentrations in premedicated patients compared to unpremedicated patients, and in patients given temazepam compared with trimeprazine, could be due to the presence of calorific substances in the syrups used as vehicles for the premedicant drugs. Temazepam syrup has a total calorific value of 36.4 cal/5 ml and contains glycerol 50%w/v, sorbitol 45%w/v and ethanol 9%w/v; trimeprazine syrup has a total calorific value of 11.36 cal/5 ml and contains 56.8%w/v sucrose. It may also be relevant that trimeprazine syrup was given 2 hours before surgery, whereas temazepam was given 1 hour pre-operatively.

The absence of hypoglycaemia in patients in the present study is in agreement with the findings of others.[2,3,10] However, caution must be exercised when comparing the results of different studies, as the glucose-specific methods of analysis require the preparation of known standards for comparison, and blood glucose measurements may vary over a period of time in the same laboratory, and from one laboratory to another. Most authors accept the definition of hypoglycaemia used in the present study, (i.e. a blood glucose of less than 2.2 mmol/litre), but others have defined hypoglycaemia as a blood glucose of less than 2.8 or 3.0 mmol/litre[11,12] and, as a result, report an incidence of pre-operative hypoglycaemia in healthy children. In our study, a blood glucose of less than 3.0 mmol/litre occurred intra-operatively in one patient (1.8%) operated on in the afternoon.

A third problem in comparing results is the inclusion of large numbers of infants and children below normal weight in some previous studies.[9,12,13] While the results of these studies may indicate that very young or underweight children are at increased risk of developing hypoglycaemia following routine pre-operative fasting they do not reflect the incidence of pre-operative hypoglycaemia in normal pre-school children.

In view of the high incidence of hypoglycaemia in his study, Thomas[1] advocated that milk feeds be given to children 4 hours pre-operatively. Other recommendations followed which included, for example, that maltose drinks should be given 2 hours pre-operatively, followed by an intramuscular injection of metoclopramide.[14] Our results indicate that pre-operative fasting prior to both morning and afternoon surgery is well tolerated in healthy pre-school children, and precautions against hypoglycaemia may be unnecessary. However, it would seem desirable from the point of view of patient comfort and hydration to keep the duration of pre-operative starvation to a minimum. At present, patients in this hospital are not allowed food for 6 hours before operation. Clear fluids are encouraged up to 4 hours pre-operatively.

Acknowledgments

We thank the nurses on the surgical wards and the laboratory staff at the Royal Manchester Childrens' Hospital for their valuable help during the study.

References

1. THOMAS DKM. Hypoglycaemia in children before operation: its incidence and prevention. *British Journal of Anaesthesia* 1974; **46:** 66–8.
2. GRAHAM IFM. Preoperative starvation and plasma glucose concentrations in children undergoing outpatient anaesthesia. *British Journal of Anaesthesia* 1979; **51:** 161–4.
3. JENSEN BH, WERNBERG M, ANDERSEN M. Preoperative starvation and blood glucose concentrations in children undergoing inpatient and outpatient anaesthesia. *British Journal of Anaesthesia* 1982; **54:** 1071–4.
4. TRINDER P. Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. *Annals of Clinical Biochemistry* 1969; **6:** 24–7.
5. CORNBLATH M, SCHWARTZ R. *Disorders of carbohydrate metabolism in infancy*, 2nd edn. Philadelphia: WB Saunders, 1976; p. 345.
6. WHICHELOW MJ, STURGE RA, KEEN H, JARRETT RJ, STIMMLER L, GRAINGER S. Diurnal variation in response to intravenous glucose. *British Medical Journal* 1974; **268:** 488–91.
7. GIBSON T, JARRETT RJ. Diurnal variation in insulin sensitivity. *Lancet* 1972; **2:** 947–8.
8. GANONG WF. *Review of medical physiology*, 8th edn. Los Altos, California: Lange Medical Publications, 1977; 267–8.
9. FFOULKES-CRABBE DJO, JOHNSON TO. Effect of anaesthesia and surgery on blood sugar and carbohydrate tolerance in African children. *Canadian Anaesthetists' Society Journal* 1976; **23:** 486–91.
10. SCHNEIDER BM, NAHRWOLD ML. Fasting plasma glucose in children. *Anesthesiology* 1982; **57:** A430.
11. ALLISON CW, CATER JI, GRAY IG, STAZIKER AC. Pre-operative starvation in children. The role of alanine in blood glucose homeostasis. *Anaesthesia* 1982; **37:** 274–7.
12. PAYNE K, IRELAND P. Plasma glucose in the perioperative period in children. *Anaesthesia* 1984; **39:** 868–72.
13. MORRICE JJ, TAYLOR KM, BLAIR JI, YOUNG DG. Preoperative plasma glucose level. *Archives of Disease in Childhood* 1974; **49:** 898–900.
14. FRY ENS, IBRAHIM AA. Hypoglycaemia in paediatric anaesthesia: the influence of metoclopramide and oral maltose in paediatric surgical patients. *Anaesthesia* 1976; **31:** 552–4.

Anaesthesia, 1986, Volume 41, pages 276–281

Midazolam in conservative dentistry

A cross-over trial

R. A. DIXON, C. KENYON, D. R. G. MARSH AND J. A. THORNTON

Summary

In a double-blind trial, 50 patients were randomly allocated to receive up to 0.29 mg/kg diazepam (Valium 5 mg/ml) or 0.14 mg/kg of midazolam (midazolam hydrochloride 5 mg/ml) intravenously at a first session of conservative dentistry, the alternative being administered at the second session. Good operating conditions were reported under each sedative and no important physiological differences were observed. Most patients failed to return to 'street fitness' 30 minutes after either session of treatment. Previous reports of reduced incidence of venous thrombophlebitis with midazolam were not convincingly confirmed in this trial, but data quality was poor. For about half the patients, the amnesic effect was stronger following midazolam.

Key words

Hypnotics, benzodiazepines; midazolam, diazepam.
Anaesthesia; dentistry.

The ideal sedative for use in conservative dentistry would provide good operating conditions, complete safety of the airway and rapid recovery, with the patient free from side or after effects. Diazepam has been used for some years for this purpose, but has fallen short of the ideal because of the relatively slow return to street fitness and also because of the high frequency of thrombophlebitis.

Midazolam is a 1.4 benzodiazepine derivative, which has been shown to be an effective intravenous induction agent[1-4] and premedicant.[1] It has anterograde amnesic properties[5,6] and, because it is water soluble, it is less likely than diazepam to cause a burning sensation on injection. It is more rapid in onset than diazepam, with less individual variation in response to a given dosage[2] and has a shorter activity.[3] Its amnesic and sedative effects in subanaesthetic doses were expected to be useful in outpatient conservative dentistry.

Patients

In a double-blind trial, 50 patients were randomly allocated to receive either diazepam (Valium 5

R.A. Dixon, BSc, PhD, Senior Lecturer in Medical Statistics, University of Sheffield Medical School, Beech Hill Road, Sheffield S10 2RX, C. Kenyon, BDS, Dental Surgeon, Department of Restorative Dentistry, Charles Clifford Dental Hospital, Wellesley Road, Sheffield S10 2SZ, D.R.G. Marsh, MB, ChB, D Obst RCOG, FFARCS (Ireland)*, Senior Registrar, Department of Anaesthetics, University of Sheffield Medical School, Beech Hill Road, Sheffield S10 2RX, Professor J.A. Thornton, MD, FFARCS, DA†, Department of Anaesthetics, University of Sheffield Medical School, Beech Hill Road, Sheffield S10 2RX.

*Present position: Consultant, Division of Anaesthesia, Southern Glasgow Hospital, Glasgow G51 4TF.

†Present address: Department of Anaesthesia, The Chinese University of Hong Kong, Shatin, NT, Hong Kong.

0003–2409/86/030276 + 06 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

mg/ml, up to 0.29 mg/kg) or midazolam hydrochloride (5 mg/ml: up to 0.14 mg/kg) at a first session of conservative dentistry, the alternative being administered at a second session one week later. The maximum doses were chosen to correspond to a maximum dose for a 70-kg man of 4 ml diazepam or 2 ml midazolam. The main aim of the trial was to compare side and after effects, but comparisons were also to be made of physiological changes, operating conditions and postoperative recovery, using methods tested in a previous trial.[7]

There were 14 male and 36 female patients whose ages ranged from 16–63 years (mean 29 years) and body weights from 47–100 kg (mean 65 kg). All patients were drawn from the waiting list for conservative dentistry at the Charles Clifford Dental Hospital, Sheffield, required at least 60 minutes of treatment without oral surgery, and were considered fit for general anaesthesia. Informed consent was obtained and no food or water was to have been consumed in the 4 hours preceding treatment. The conservation work planned for each session was expected to last for 30 minutes for cavity preparation and filling. Patients were in the semi reclined position and a cellulose mouth pack was used.

Of the 24 patients who received diazepam at the first session, all but two returned for a second session on midazolam; of the 26 who received midazolam first, all but three returned for the diazepam session. Thus, there were 47 diazepam and 48 midazolam sessions and 45 patients completed both sessions.

A single dose of the respective drug was administered through an antecubital vein (left arm at first session, right arm at second, wherever possible) at a rate of 1 ml/minute up to the intended weight-related dose, to the nearest 0.2 ml, unless over-sedation was previously indicated by drooping of the eyelids and/or loss of consciousness and/or withdrawal and/or any loss of verbal contact. Patients who weighed over 70 kg received a maximum dose corresponding to an assumed weight of 70 kg (i.e. 4 ml diazepam or 2 ml midazolam). The actual dosage of diazepam administered ranged from 0.10–0.30 mg/kg (mean 0.27 mg/kg); five patients received under 90% of the intended weight-related dose. Four patients received under 90% of the intended dose of midazolam, one incorrectly received more than 110% of the intended dose and the dosage ranged from 0.08–0.16 mg/kg (mean 0.14 mg/kg). The identity of the sedative was not revealed to the dental surgeon (administered out of his sight), but it was not possible for the anaesthetist to administer the trial sedatives on a blind basis.

Physiological monitoring was carried out by a technician using a Dinamap automatic blood pressure measuring device, an ear oximeter, an ECG (lead II) and a mercury strain gauge. Readings were taken immediately before the intravenous sedation, one minute after completion of sedation, one minute after administration of the local analgesic and at 5 minute intervals thereafter. Immediate postoperative recovery was assessed by the deletion of letters[7] test, 10, 20 and 30 minutes after the end of dental treatment.

Patients' amnesic experience was assessed 40 minutes after the intravenous sedative by the anaesthetist who asked the patients if they remembered the injection and, if so, which one to determine if amnesia is effective from before or after the sedative or not even then. Also, one week after each treatment session, patients were asked if they remembered their fillings being done very clearly, vaguely or not at all.

Arm pain and venous thrombophlebitis were assessed one week after treatment. Patients were asked at this time whether they had experienced arm soreness after leaving the hospital, and the anaesthetist at the same time examined the venepuncture site. Thrombophlebitis was defined as redness and/or a palpable cord.

The incidence of other possible after effects (drowsiness, unsteadiness, forgetfulness) was also assessed one week after each treatment session in a self administered questionnaire. On the second occasion, patients also had an opportunity to express a slight or strong preference for the sedative used at the first or second session.

Results

Operating conditions

One dental surgeon (CK) carried out all the conservative dentistry and assessed the operating conditions (blind) as 'good', 'acceptable' or 'unacceptable' under four specific headings (Table 1) and also gave his overall impression. Thirty-four diazepam (72%) and 33 midazolam (69%) sessions gave a good overall impression. Nine of the 45 patients who underwent both sessions were classified differently on the two occasions and five of the nine were given a better classification on

Table 1. Operating conditions

	% of sessions assessed as 'good'		Number of patients assessed differently at two sessions ($n = 45$)	Of those patients assessed differently, number given better assessment at diazepam session
	Diazepam ($n = 47$)	Midazolam ($n = 48$)		
Ease of administration of local analgesic	83	83	7	2
Tongue movement	81	81	4	3
Patient movement	79	81	6	2
Ease of access	68	65	14	9
Overall impression (dental surgeon)	72	69	9	5

Table 2. Adverse physiological events.* ($n = 45$)

	No. of patients
One or more physiological events at *both* sessions	6
One or more events at one session but none at the other:	
event(s) at diazepam session only	2
event(s) at midazolam session only	4
No event at either session	16
Monitoring information missing (one or more of the six sources; one or both sessions)	17†

*Systolic blood pressure increase/decrease ⩾ 30 mmHg; pulse rate increase/decrease ⩾ 40 bpm; oxygen saturation decrease ⩾ 5%; apnoea lasting ⩾ 30 seconds; verbal contact lost for ⩾ 30 seconds; respiratory obstruction.

†In addition, some data were missing for some of the six patients counted in the first row of the table, but this does not affect their appropriate placement in the table.

diazepam than on midazolam. Individual aspects of the operating conditions also gave comparable assessments under each sedative.

Thirteen different anaesthetists, each involved in about as many diazepam as midazolam sessions, reported adverse effects. Partial airway obstruction or snoring was noted at five midazolam but no diazepam sessions. Excessive drowsiness was noted at seven midazolam but only one diazepam session. Less common reactions (1–3 reports per sedative) for both diazepam and midazolam were difficulty in keeping mouth open, weeping, irritation in throat, excessive coughing and irritability. For diazepam only, painful injection and retching were noted and for midazolam only, dizziness, unpleasant taste, apnoea and diplopia.

Physiological monitoring

The ear oximeter failed to function adequately at 12 diazepam and 11 midazolam sessions. Other equipment failure affected another four diazepam and four midazolam sessions. Six of the 45 patients undergoing both sessions experienced one or more physiological events at both sessions (Table 2). For another 17 patients, monitoring information was incomplete and 16 patients completely monitored experienced no event. Of the six who experienced one or more events at one session but none at the other, though completely monitored, four experienced their event(s) on midazolam.

Amnesia

Of the 45 patients treated at both sessions, 33 had a similar experience of amnesia on the two occasions; one patient could on each occasion remember, 40 minutes after the sedative, both the intravenous and local injections, 31 could remember only the intravenous injection and one could remember neither. For another three patients, inadequate information was recorded, and the remaining nine gave different responses following the two sedatives; for six of these the

Table 3. Arm pain and venous thrombophlebitis

	Diazepam $n = 47$ (100%)	Midazolam $n = 48$ (100%)
	%	%
Arm pain reported during week following treatment		
Yes	21	15
No	70	77
Not known	9	8
Thrombophlebitis on examination one week after treatment		
Yes	19	4
No	60	73
Not known	21	23
Arm pain and/or thrombophlebitis		
Yes	36	15
No	49	65
Not known	15	20

Table 4. After effects recalled one week after treatment

	% of patients following		Number of patients giving different reply after diazepam that following midazolam	Of number giving different reply, number showing after-effect following diazepam only
	Diazepam ($n = 47$)	Midazolam ($n = 48$)		
Drowsiness	66	82	16	4
Unsteadiness	50	55	13	5
Forgetfulness	30	43	14	4
'Not usual self' in 48 hours following treatment	25	27	10	4

amnesic response was stronger with midazolam.

An answer was recorded for 41 patients, one week following each sedative, to the question How clearly do you remember your fillings being done? For 16 patients identical answers were recorded on the two occasions (vaguely, 8; not at all, 8) but of 25 giving differing responses, 21 remembered less clearly on midazolam ($p < 0.01$, Sign test).

Immediate postoperative recovery

Of 45 patients completing both sessions, 11 (24%) had recovered, according to the deletion of letters test, by 30 minutes after the end of dental treatment following diazepam, and four (9%) following midazolam. Comparison of the test results at 10, 20 and 30 minutes following each session shows that 32 patients had not recovered by 30 minutes after either sedative; one patient recovered at 20 minutes after each sedative; 12 patients recovered at different times, of whom nine recovered earlier following diazepam.

Arm pain and venous thrombophlebitis

Information on postoperative arm pain (Table 3) was missing following four diazepam and four midazolam sessions. Some patients did not attend for their second session of treatment and some failed to return one week after that. Thus, the observed incidence was at least 21% following diazepam and at least 15% following midazolam. For similar reasons, and because of the occasional unavailability of an anaesthetist for the sole task of inspecting the venepuncture site one week after the second treatment session, information on the presence or absence of venous thrombophlebitis is even more scanty. The observed incidence one week after diazepam was at least 19% and after midazolam at least 4%, but information is missing for over 20% of the sessions.

Combining the arm pain symptom with the signs of thrombophlebitis, the observed incidence is at least 36% for diazepam, and at least 15% for midazolam. Using this combined definition of thrombophlebitis, it was possible to compare 33 patients following both sedatives: 19 gave the same result following each sedative (present 5; absent 14); of the 14 showing different results, 11 showed thrombophlebitis present only following diazepam ($p > 0.05$, Sign test).

After effects

For similar reasons, information on after effects was not obtained from all patients and the observed incidences shown in Table 4 are therefore likely to be underestimates. The last two columns, however, show that when patients experienced an after effect following one sedative but not the other, it more frequently involved midazolam.

Preferred sedative

Of 40 patients asked by questionnaire one week after the second treatment to express a preference for the first or second sedative, 32 did so (Table 5). The expected preference[7-9] for the first sedative (preferred by 22 of the 32, or by 16 of the 21 having a strong preference) was more convincing than the small preference for midazolam. Of the 32 expressing any preference, 20 preferred midazolam ($p > 0.05$, Sign test); of the 21 expressing a strong preference, 14 preferred midazolam ($p > 0.05$, Sign test).

Table 5. Preferred sedative ($n = 40$)

First sedative: strong preference	16	22
slight preference	6	
No preference		8
Second sedative: slight preference	5	10
strong preference	5	
Diazepam: strong preference	7	12
slight preference	5	
No preference		8
Midazolam: slight preference	6	20
strong preference	14	

Discussion

In this trial, the dental surgeon assessed the operating conditions overall as good following the majority of midazolam sessions and diazepam sessions alike, though partial airway obstruction was recorded by the anaesthetist at some of the midazolam sessions. Failure of equipment led to inadequate physiological monitoring data, but there was no evidence of any difference between the sedatives in the occurrence of adverse physiological events during sedation.

The more rapid recovery expected following midazolam[10,11] was not demonstrated, as compared with the results of Kawar *et al.*[12] Two thirds of patients remained unrecovered 30 minutes after the end of *both* sessions of treatment, and after effects like drowsiness, unsteadiness and forgetfulness were, if anything, more common following midazolam.

In a study on midazolam for endoscopy, a significant prolongation of reaction time, up to 2.5 hours after injection, was demonstrated.[13] In that study, the possibility of initial partial recovery at 15 minutes after injection followed by resedation at 75 minutes post injection was considered. No significant difference in recovery was demonstrated between the drugs, up to 3 hours following injection, in a study comparing midazolam and diazepam as sedation during spinal anaesthesia.[14]

Difficulties were experienced in following up patients to elicit signs and symptoms of thrombophlebitis at the venepuncture site. Anaesthetic service requirements prevented the deployment of an anaesthetists solely for this function, so that this task was carried out at times convenient to an anaesthetist giving general anaesthetics for dental extractions in an adjoining room. Perhaps the inadequate quality of our data from this relatively small trial has prevented us from clearly confirming the reduction of arm pain/thrombophlebitis found with midazolam compared to diazepam, found in two earlier studies.[10,11] The introduction of diazepam in oil (Diazemuls), however, may diminish the importance of confirming this finding.

The most clearly confirmed difference between the two sedatives was the more profound amnesia associated with midazolam.[15] Amnesia is a particularly useful effect in conservative dentistry, since it is often fear of the local anaesthetic injection which is most troublesome.

Our dosage schedules both for midazolam (0.14 mg/kg), determined in a pilot study, and for diazepam (0.29 mg/kg), were higher than those used by Al-Khudhairi *et al.*[11] in their study of both these drugs as sedation for gastroscopy. Perhaps higher levels of anxiety are experienced in patients presenting for conservative dentistry? Dundee *et al.*[10] drew attention to the great individual variation in response to benzodiazepines, including midazolam, which appears not to be related to weight. In our trial, only one patient who received midazolam exceeded the intended weight related dose by more than 10%. The expressed preference of the patients for the first sedative administered, found in previous trials, was confirmed here more convincingly than a tendency to prefer midazolam.

In conclusion, with the introduction of diazepam in an emulsion (Diazemuls) since this trial was planned, we see insufficient evidence from this trial taken in the context of other reported studies, for clinicians to choose midazolam in preference, unless the improved amnesic effect is wanted.

References

1. Conner JT, Katz RL, Pagano RR, Graham CW. RO 21-3981 for intravenous surgical premedication and induction of anaesthesia. *Anesthesia and Analgesia* 1978; **57:** 1–5.
2. Reves JG, Corssen G, Holcomb C. Comparison of two benzodiazepines for anaesthesia induction: midazolam and diazepam. *Canadian Anaesthetists' Society Journal* 1978; **25:** 211–4.
3. Brown CR, Sarnquist FH, Pedley TA. RO 21-2981: clinical, electroencephalographic and pharmacokinetic study (abstract). *Annual Meeting of the American Society of Anesthesiologists* 1977, p. 241.
4. Fragen RJ, Gahl F, Caldwell N. RO 21-3981 for induction of anaesthesia. A water-soluble benzodiazepine. *Anesthesiology* 1978; **49:** 41–3.
5. Forster A, Gardaz JP, Suter PM, Gemperle M. I.V. midazolam as an induction agent for anaesthesia: a study in volunteers. *British Journal of Anaesthesia* 1980; **52:** 907–11.
6. Dundee JW, Wilson DB. Amnesic action of midazolam. *Anaesthesia* 1980; **35:** 459–61.
7. Dixon RA, Bennett NR, Harrison MJ, Kenyon C, Thornton JA. I.V. flunitrazepam and I.V. diazepam in conservative dentistry: a cross-over trial. *British Journal of Anaesthesia* 1980; **52:** 517–26.
8. Cossham PS, Dixon RA. Subanaesthetic dosage of propanidid as a sedative for dentistry: a controlled clinical trial. *British Journal of Anaesthesia* 1973; **45:** 369–75.
9. Dixon RA, Atkinson RE, Kenyon C, Lamb D, Thornton JA, Woodhead S. Subanaesthetic dosage of Althesin as a sedative for conservative dentistry: a controlled trial. *British Journal of Anaesthesia* 1976; **48:** 431–9.
10. Dundee JW, Samuel IO, Toner W, Howard PJ. Midazolam: a water-soluble benzodiazepine. Studies in volunteers. *Anaesthesia* 1980; **35:** 454–8.
11. Al-Khudhairi D, Whitwam JG, McCloy RF. Midazolam and diazepam for gastroscopy. *Anaesthesia* 1982; **37:** 1002–6.
12. Kawar P, Gamble JAS, Browne ES, Dundee JW. Midazolam as a sedative in dentistry. *British Journal of Anaesthesia* 1982; **54:** 1137.
13. Ruiz K, Asbury AJ, Thornton JA. Midazolam—does it cause resedation? *Anaesthesia* 1983; **38:** 898–902.
14. McLure IH, Brown DT, Wildsmith JAW. Comparison of the I.V. administration of midazolam and diazepam as sedation during spinal anaesthesia. *British Journal of Anaesthesia* 1983; **55:** 1089–93.
15. McGimpsey JG, Kawar P, Gamble JAS, Browne ES, Dundee JW. Midazolam in dentistry. *British Dental Journal* 1983; **155:** 47–50.

Anaesthesia, 1986, Volume 41, pages 282–286

Intubating conditions following pre-induction priming with alcuronium

A. W. HARROP-GRIFFITHS, R. M. GROUNDS AND M. MOORE

Summary

Three priming doses of alcuronium have been investigated and, using a logistic transformation technique, the priming dose required to produce adequate intubating conditions in 99% of patients at 60 seconds following the second dose of alcuronium has been deduced. This dose, 106.5 μg/kg is extremely high and may be unsafe if used, since 30% of our patients complained of side effects when given a priming dose of only 50 μg/kg.

Key words

Neuromuscular relaxants; alcuronium.

There has been much recent interest in the priming principle for non-depolarising neuromuscular blocking drugs.[1–4] Foldes[5] has recommended the use of a priming dose, followed after a short interval by a second, larger intubating dose administered at the same time as the intravenous induction agent. He proposed that the priming dose should be large enough to cause moderate inhibition of neuromuscular transmission, indicating greater than 75% occupancy of the endplate receptors.[6] Using this technique, it should be possible, theoretically, to achieve adequate intubating conditions in 99% of patients within 60 seconds of induction and the injection of the intubating dose. This should be achieved without the patient suffering any unpleasant side effects and, more importantly, without the loss of protective laryngeal reflexes.

In the present study, we have used a single-blind technique to investigate the validity of these statements. We have examined the effects of several different priming doses of alcuronium on the adequacy of intubation at 60, 90 and 120 seconds after the second dose of alcuronium. The study was designed to determine the priming dose required to achieve adequate intubating conditions in 99% of cases within 60 seconds of giving the intubating dose of alcuronium.

Methods

Forty healthy female patients about to undergo routine elective gynaecological surgery and requiring tracheal intubation as part of the anaesthetic technique were studied. Their ages ranged between 25 and 57 years. No patient with a history of difficulties at laryngoscopy was studied. The patients were seen prior to their proposed time of surgery, the technique explained to them and their written informed consent obtained.

All patients were premedicated with atropine

A. W. Harrop-Griffiths, MB, BS, FFARCS, Registrar, R.M. Grounds, MB, BS, FFARCS, Senior Registrar, Department of Anaesthetics, Hammersmith Hospital, Du Cane Road, London W12 0HS, M. Moore, MSc, Statistician, Department of Medical Statistics, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT.

0003–2409/86/030282 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

0.6 mg intramuscularly, approximately one hour prior to operation. They were randomly divided into four groups of ten patients each. Group 1 received 1 ml of normal saline priming dose and 200 μg/kg alcuronium as the intubating dose; group 2 received 20 μg/kg alcuronium as the priming dose and 180 μg/kg alcuronium as the intubating dose; group 3 received 35 μg/kg as the priming dose and 165 μg/kg as the intubating dose, while group 4 received 50 μg/kg as the priming dose and 150 μg/kg as the intubating dose.

On arrival in the anaesthetic room a cannula was inserted into a forearm vein and the priming dose injected into a fast-running intravenous infusion. A stopwatch was started on completion of the injection of the priming dose, and when 2 minutes had elapsed, a dose of thiopentone 4 mg/kg was injected over 20 seconds followed by the intubating dose of alcuronium over 10 seconds, again with the infusion running rapidly. Timing recommenced at the end of the injection of the alcuronium. The patients' lungs were then ventilated with nitrous oxide 6 litres/minute and oxygen 3 litres/minute and halothane 1% to within 5 seconds of the required time to test the intubating conditions, (55 seconds after intubating dose). Intubation was attempted at 60, 90 and 120 seconds. Only orotracheal intubations were attempted and all were performed by one of the authors, (RMG), who was unaware of the priming or intubating doses used, and only knew that all patients had received a total of 200 μg/kg of alcuronium.

The patients were assessed subjectively for jaw relaxation, vocal cord relaxation and suitability for atraumatic laryngoscopy. Intubating conditions were assessed according to a modified scheme used by Harrison and Feldman,[7] originally proposed by Lund and Stovner.[8]

Statistical methods

Logistic transformation was used to analyse the data and to provide an estimation of the priming dose required to ensure adequate intubating conditions in 99% of cases. The estimation procedure has been described by Armitage,[9] and is discussed in detail, for this particular study, in the appendix to the paper.

Results

The mean ages and weights of the four groups of patients are shown in Table 1. There was no statistical difference between the groups for age or weight. Table 2 shows the incidence of jaw and cord relaxation and success of attempted intubation. Figure 1 illustrates the intubating conditions at 60, 90 and 120 seconds after the second or intubating dose of alcuronium.

Table 1. Age and weight of patients in the four different priming groups (mean, SD)

	Group			
	1	2	3	4
Alcuronium priming dose (μg/kg)	0	20	35	50
Mean weight (kg)	65.7	64.00	62.4	58.5
	(8.8)	(15.1)	(9.5)	(12.2)
Mean age (years)	37.3	36.2	35.8	33.4
	(8.1)	(3.9)	(9.0)	(4.6)

Jaw relaxation

After 60 seconds, only those patients who had received 50 μg/kg priming dose were all considered to have satisfactory jaw relaxation for a safe, successful intubation. By 120 seconds, even those who had not received a priming dose were considered to have sufficient jaw relaxation to allow safe, atraumatic insertion of the laryngoscope.

Cord relaxation

At 60 seconds no group had 100% of patients in whom relaxation was considered adequate for safe atraumatic intubation. The best group was the one in which patients had all received a priming dose of 50 μg/kg of alcuronium. By 120 seconds, cord relaxation was considered adequate in all groups except those that had not received a priming dose of alcuronium.

Statistical analysis

Separate analyses were performed for each of the three time periods, using the Generalised Linear Interactive Modelling package (GLIM) of the Royal Statistical Society. On the basis of χ^2 (with two degrees of freedom) test for heterogeneity, the model, as described in the appendix, fitted each set of data very well.

The estimates of intercept and slopes together with the χ^2 values are shown in Table 3. In Table 4, the ED_{99} and corresponding estimate of initial

Table 2. Incidence of degrees of jaw and cord relaxation and success of attempted intubation(s)

	Time of attempted intubation(s)											
	60 seconds				90 seconds				120 seconds			
Alcuronium priming dose (μg/kg)	0	20	35	50	0	20	35	50	0	20	35	50
Jaw relaxation												
satisfactory	6	6	8	10	8	9	10	10	10	10	10	10
unsatisfactory	4	4	2	0	2	1	0	0	0	0	0	0
Cord relaxation												
satisfactory	4	6	5	9	7	10	10	10	7	10	10	10
unsatisfactory	6	4	5	1	3	0	0	0	3	0	0	0
Tracheal intubation												
successful	4	5	5	9	7	9	10	10	8	10	10	10
unsuccessful	6	5	5	1	3	1	0	0	2	0	0	0

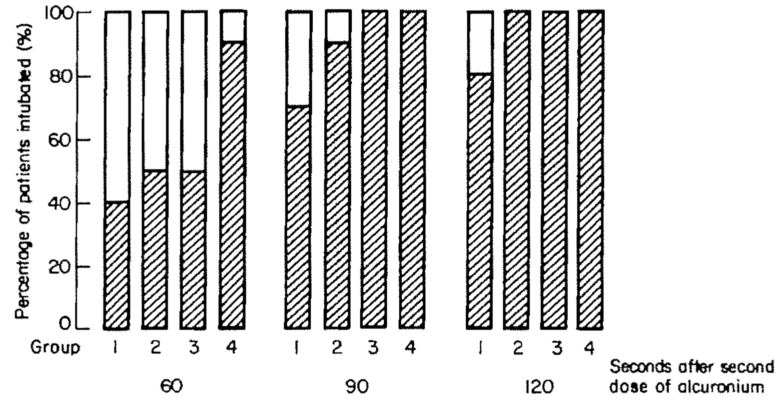


Fig. 1. Intubating conditions at different times for the four groups studied. ■, Satisfactory; □, unsatisfactory. Group 1, 0 μg/kg; group 2, 20 μg/kg; group 3, 35 μg/kg; group 4, 50 μg/kg.

Table 3. Estimates of slope and intercept and Chi square values

Time after second dose of alcuronium	Intercept $\hat{\alpha}$	Slope β	Chi-square χ^2
60 seconds	35.93	−15.9	2.12
(SD)	(17.28)	(7.71)	
90 seconds	95.49	−41.16	0.53
(SD)	(50.04)	(21.9)	
120 seconds	390.7	−169.2	0.002
(SD)	(922.9)	(401.1)	

Table 4. Estimates of priming doses required to provide adequate intubating conditions in 99% of cases at 60, 90 and 120 seconds

Time of attempted intubation following second dose of alcuronium	ED$_{99}$	Estimate of priming dose of alcuronium required for 99% satisfactory conditions (μg/kg)
60 seconds	1.97	106.5
90 seconds	2.21	38.6
120 seconds	2.28	9.5

dose required for 99% successful intubation at 60, 90 and 120 seconds are shown. The estimated priming dose that would allow 99% successful intubation at 60 seconds was 106.5 μg/kg However, at the 50 μg/kg priming dose, 30% of patients complained of unpleasant side effects attributable solely to alcuronium. These included a 'dreadful' feeling of weakness and heaviness of the eyelids, and one patient was completely unable to open her eyes.

Discussion

The ability rapidly and safely to intubate the trachea is still paramount in emergency anaesthesia, where the possibility exists that the patient may have a full stomach, and many anaesthetists still use suxamethonium for this purpose. Tracheal intubation can usually be performed within 60 seconds of suxamethonium administration. This drug has many side effects, some of which are minor and can be prevented. However, it cannot be used safely in severely burned patients,[10] or in patients with myotonia[11] or in patients susceptible to malignant hyperthermia. It is also relatively contraindicated in patients with renal failure,[12] severe liver disease and penetrating injuries of the eye. For these and other reasons, the search for an alternative drug to suxamethonium, or an alternative method of using the non-depolarising neuromuscular blocking agents for use in a rapid sequence induction to intubation technique, has been sought.

The fact that a priming dose of non-depolarising relaxants, given some minutes prior to the main dose, can shorten the time taken to achieve adequate intubating conditions has been demonstrated in a number of studies.[1-4] However, if as suggested by Foldes and his co-workers,[1,5] this technique is seriously to compete with the use of suxamethonium, then it must be shown to produce results comparable with the use of suxamethonium.

Foldes[5] has recommended that a priming dose of alcuronium should be 45–60 μg/kg, followed by an intubating dose of 150–180 μg/kg. This study has shown that the priming dose recommended by Foldes[5] was accompanied by a 30% incidence of side effects which were unacceptable to the patient. Hutton *et al.*[13] studied a priming dose of alcuronium and showed that it shortened the time elapsed for successful intubation following the main dose of alcuronium, but did not demonstrate any side effects from the priming dose because their patients were all anaesthetised with thiopentone prior to being given the priming dose. We have also shown that even with a 'priming' dose of 50 μg/kg only 90% of our patients could be safely and successfully intubated at 60 seconds, whereas to compete seriously with suxamethonium, we would have expected 99% of the patients to be intubated within 60 seconds of injection of alcuronium.

We have estimated the priming dose which would ensure adequate intubating conditions in 99% of patients after 60 seconds by the use of logistic transformation. This dose was 106.5 μg/kg. (7.5 mg alcuronium for 70 kg patients). Since 30% of our patients suffered side effects with the 50 μg/kg dose, we considered it unacceptable to more than double the priming dose in our patients.

Gergis[14] and colleagues allowed 3 minutes to elapse between the injection of the priming and intubating doses, while Foldes[5] recommended allowing 6–8 minutes between the two doses. We suggest that there are good reasons why the longer time between doses should be avoided. Firstly, the longer time may allow greater numbers of patients to develop minor side effects such as a feeling of weakness and the inability to open their eyes. Secondly, and more importantly, the longer time delay between the two doses may allow the development of a dangerous degree of relaxation to occur with alcuronium, so that the patient may become hypoxaemic or lose laryngeal reflexes. Thirdly, a 6–8 minute delay is unacceptable in emergency anaesthesia.

We do not recommend the use of alcuronium in a two dose technique for rapid sequence tracheal intubation. However, at present we have no experience of the use of this technique with other neuromuscular blocking agents. Gergis *et al.*[14] have reported the use of this technique using atracurium, but their patients were induced with fentanyl and thiopentone followed by 70% nitrous oxide in oxygen administered by facemask one minute before the intubating dose of atracurium was given. We conclude that there is little justification for the use of the priming technique to facilitate rapid tracheal intubation.

Appendix

Ordinary regression analysis cannot be employed in the analysis of the results of this study, since standard regression analysis assumes that the dependent variable is continuous and that it is normally distributed. In this case, we have a sigmoid log dose/response curve of $\log_{10}$ priming dose against response, i.e. percentage intubated at 60 seconds (or 90 or 120 seconds). However, the result we are interested in is the $\log_{10}$ dose at the 99% response, i.e. the top right hand end of the sigmoid curve, and it is not always easy to determine this point accurately. The logistic transformation is a commonly applied method in such circumstances. This technique enables a sigmoid $\log_{10}$ dose/response curve to be transformed into a straight line relationship with dose. The transformation is

$$y = \log_e \frac{(\quad P \quad)}{1-P}$$

$$\text{and } y = \alpha + \beta x$$

where p = proportion intubated at x
$x = \log_{10}$ dose
$y = y$ axis of graph
α = intercept on y axis
β = slope of transformed line.

This estimation procedure has been well documented by Armitage[9] and Petrie.[15]

In this case, the point of interest is the log dose at which intubation can be achieved in 99% of cases. The logit value at this points

$$Y_{99} = \log_e \frac{(0.99)}{(0.01)} = \log_e (99) = 4.595$$

so that the effective log dose giving 99% response

$$\text{is } E_{D99} = \frac{4.595 - \alpha}{\beta}$$

References

1. Foldes FF, Schwarz S, Ilias W, Lackner F, Nagashima H, Mayerhofer O. Rapid tracheal intubation with vecuronium: the priming principle. *Anesthesiology* 1984; **61:** A294.
2. Mehta MP, Choi WW, Gergis SD, Sokoll MD. Faster onset of neuromuscular blockade with non-depolarizing muscle relaxants. *Anesthesiology* 1984; **61:** A311.
3. Bevan JC, Doherty WG, Breen PG, Donati F, Bevan DR. Accelerated onset of pancuronium neuromuscular block with divided doses in infants and children. *Anesthesiology* 1984; **61:** A312.
4. Nagashima H, Nguyen HD, Lee S, Kaplan R, Duncalf D, Foldes FF. Facilitation of rapid endotracheal intubation with atracurium. *Anesthesiology* 1984; **61:** A289.
5. Foldes FF. Rapid tracheal intubation with non-depolarising neuromuscular blocking drugs: the priming principle. *British Journal of Anaesthesia* 1984; **56:** 663.
6. Paton WDM, Waud DR. The margin of safety of neuromuscular transmission. *Journal of Physiology* 1967; **191:** 59–90.
7. Harrison P, Feldman SA. Intubating conditions with ORG NC45. A preliminary study. *Anaesthesia* 1981; **36:** 874–7.
8. Lund I, Stovner J. Experimental and clinical experiences with a new muscle relaxant R04-3816, diallyl-nor-toxiferine. *Acta Anaesthesiologica Scandinavica* 1962; **6:** 85–97.
9. Armitage P. *Statistical methods in medical research.* London: Blackwell, 1977. 375–84.
10. Tolmie JD, Joyce TH, Mitchell GD. Succinylcholine danger in the burned patient. *Anesthesiology* 1967; **28:** 467–70.
11. Cooperman LH. Succinylcholine-induced hyperkalemia in neuromuscular disease. *Journal of the American Medical Association* 1970; **213:** 1867–71.
12. Powell JN. Suxamethonium-induced hyperkalaemia in a uraemic patient. *British Journal of Anaesthesia* 1970; **42:** 806–7.
13. Hutton P, Morgan G, El-Hassan K, Black AMS. Speeding the onset of neuromuscular block by alcuronium. *British Journal of Anaesthesia* 1983; **55:** 918P.
14. Gergis SD, Sokoll MD, Mehta M, Kemmotsu O, Rudd GD. Intubating conditions after atracurium and suxamethonium. *British Journal of Anaesthesia* 1983; **55:** 83S–6S.
15. Petrie A. *Lecture notes on medical statistics.* London: Blackwell, 1978. 130–2.

Anaesthesia, 1986, Volume 41, pages 287–293

Pressure changes in tracheal tube cuffs

M. CHANDLER

Summary

The pressure changes in tracheal tube cuffs can be explained by classical permeation theory. The transport of all gases contributes to pressure changes which may be negative or positive, depending upon the conditions. In vitro *experiments were carried out to determine the applicability of this approach and the efficacy of the methods for minimising the rise in cuff pressure.*

Key words

Equipment; tubes, tracheal.

Previous work has shown that the pressure rise in tracheal tube cuffs during nitrous oxide anaesthesia[1–4] can be explained by classical permeation theory. This increased pressure is exerted directly on the tracheal wall. Pressure on the trachea has been implicated in the development of postoperative sore throat,[5–7] and, more seriously, tracheal stenosis.[8]

Various methods have been suggested to minimise the pressure rise caused by nitrous oxide diffusion. These include filling the cuff with saline solution,[9] with the anaesthetising gas[10] and with a rediffusion system.[11] This work extends that which was previously described, to provide a theoretical analysis of such suggestions. A method is suggested, whereby the gas transport mechanisms can be calculated.

Method

In order to determine the pressure increase in tracheal tube cuffs in contact with nitrous oxide, the apparatus was set up as shown in Fig. 1.

The tracheal tube (a) was placed in a

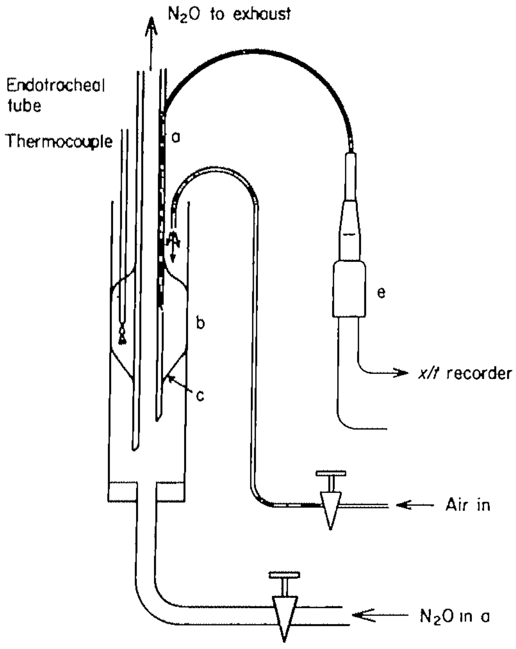


Fig. 1. Apparatus to determine pressure rise in tracheal tube cuff.

M. Chandler, MSc, Senior Product Scientist, Portex Ltd, Hythe, Kent, CT21 6JL.

0003–2409/86/030287 + 07 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Perspex tube (b) of 20.2 mm diameter (giving approximately the same cross sectional area as an average adult trachea), and the cuff (c) inflated to such an extent that all creases and folds were flattened out. The cuff was inflated using a syringe for air, and a pressure reducing valve from a gas cylinder for the other gases. Nitrous oxide (99.6 percent minimum) was passed into the bottom of the tube (d), thus bathing the lower end of the cuff and passing through the tracheal tube and out through an extractor. Air was blown over the top end of the cuff, so that it could be assumed at any time that the concentration of any gas apart from air was zero at the top of the cuff.

The pressure in the cuff was monitored using a Bell and Howell pressure transducer (e) model 4-366-0002-01m0 (0–70 kPa, output 0.50 mV–10.5 V input); the output was recorded on a Servoscribe recorder. The transducer was calibrated against a mercury U-tube manometer. The experiment was continued for 7 hours for the PVC cuffed tubes, 5.5 hours for natural rubber and 2 hours for silicone rubber.

The areas of contact with the gas, and the volume of the cuff, were calculated from the geometry of the cuff under a shadowgraph. The thickness of the cuff was measured using a micrometer. Six readings around the neck of the cuff were taken and the average and range recorded. The position of the cuff was marked on the Perspex tube at the start of the experiment and monitored throughout the experiment, to determine if any volume or shape changes occurred.

The temperature was monitored throughout the experiments by a thermocouple. The experiments were repeated in triplicate using new tubes for each test. To determine the effects of an external reservoir, the inflation balloons of 8.0 mm internal diameter tracheal tubes were removed and 'High Volume–Low Pressure' cuffs fitted in line (No 6, Table 1).

Results

The cuff/gas combinations tested are shown in Table 1 and the results obtained are shown in the corresponding Figs 2–7 (note change of scale in Fig. 6).

There was some variation in cuff thickness; the greatest was shown by the silicone rubber cuff (SD 0.01 mm). The latex cuffs had a maximum of 0.008 mm and PVC a maximum of 0.005 mm variation. The latex cuff was tested in a smaller glass tube (12.3 mm internal diameter) to ensure that stretching, and hence thinning of the cuff material was kept to a minimum.

Generally, the pressure changes showed the same form, an initial increase to a maximum, followed by a decrease in pressure. The PVC cuff filled with air, however, did not show the fall from the maximum pressure which it reached after 6 hours. The initial rise in pressure was accompanied by a slight ballooning out of the end of the cuff.

Table 1

Cuff material/ manufacturer	Cuff filling medium	Volume of cuff ml	Area Upper	Area Lower (sq cm)	Mean thickness (cm) Upper	Mean thickness (cm) Lower	Temp (°C)	Results
PVC*/Portex 8.0 mm ID high volume cuff	Air	4.4	4.42	3.58	0.0250	0.0250	21	Fig. 2
Latex/rubber**/Leyland 7.0 mm ID	Air	0.59	0.37	0.37	0.0250	0.0250	21	Fig. 3
Silicone rubber/Dover 8.0 mm ID	Air	3.3	1.10	0.89	0.0250	0.0250	21	Fig. 4
PVC*/Portex 8.0 mm ID high volume cuff	N_2O	4.4	4.42	3.58	0.0250	0.0250	21	Fig. 5
PVC*/Portex 8.0 mm ID high volume cuff	CO_2	4.34	5.92	4.82	0.0250	0.0250	20	Fig. 6
PVC/Portex 8.0 mm ID high volume cuff	Air	4.4 + 6.00	4.40 + 14.5	3.6	0.0250	0.0250	21	Fig. 7

*Inflation pilot balloon removed.

**Inflated in 12.3 mm ID glass tube.

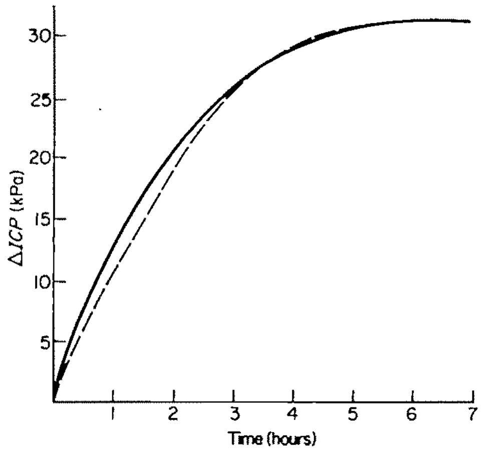


Fig. 2. Pressure changes in PVC tracheal tube cuff, filled with air, in nitrous oxide. ——, Experimental; – – –, theoretical.

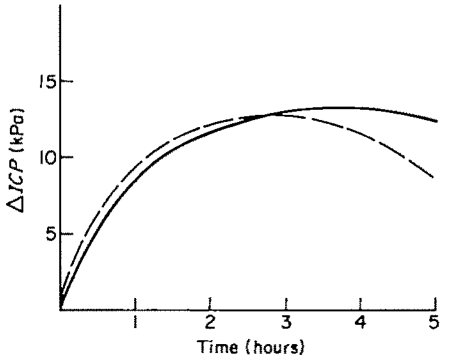


Fig. 3. Pressure changes in latex tracheal tube cuff, filled with air, in nitrous oxide. ——, Experimental; – – –, theoretical.

This resulted in a volume change of 3 percent in the case of the PVC cuff filled with air, but was less than 1 percent with the other cuffs.

When the silicone rubber cuffed tube was used, there was a loss of seal within 60 minutes. Over the same period, the length of cuff in contact with the glass tube decreased from 30 mm to less than 15 mm. This represented a change in volume of about 20 percent. There was no measurable change in contact length in any other experiment. The exception to the general pressure change behaviour was observed with the nitrous oxide filled cuff. This showed an immediate and continuing fall in pressure from the initial seal pressure. The experiment was terminated when the seal was broken. There was no measurable change in volume at this point; the loss of seal was caused by gas leaking through creases that had formed in the cuff.

All cuffs were initially sealed at deliberately high pressures (10 kPa for the PVC cuffs filled with air and 20–25 kPa for all the other tests). This was to try and ensure that all creases were removed and that a seal would be maintained throughout the experiment. If the same initial sealing pressure was used for a series of similar tubes, the pressure changes were reproducible to within 2 percent.

There was no measurable change in temperature in any other experiment.

Discussion

A brief description of the gas transport mechanism, together with a method whereby the effect may be quantified, is presented in Appendix 1. The permeability coefficients of the materials tested are shown in Table 2. Using these values in the basic equation in Appendix 1, the results are shown on their relevant graphs in Figs 2–7.

Generally, there is correspondence between the theoretical prediction and the observed behaviour. However, there are differences in the absolute values observed. One reason for this may be the assumption that the only gas transport mechanism involved is through the cuff material. There will, however, be some transport through the tube walls; this will have the effect of increasing the K_1 value in the theoretical equation by 12 percent. If this is considered, the pressures involved become similar.

The large deviation observed with the silicone rubber tube (Fig. 4) was due to change in volume of the cuff. It is noteworthy with this cuff that the pressure drops below seal pressure within one hour with loss of seal. This problem is recognised by the manufacturers, as the pack carries a warning of the need to monitor the pressure regularly. In an attempt to ensure that such a loss of seal would not introduce anomalies, deliberately high initial sealing pressures were used. Even these pressures were not enough to assure that loss of seal could not occur and the nitrous oxide filled cuff experiment (Fig. 5) was terminated because this obviously happened.

Such high initial pressure would tend to lower the initial rate of pressure increase due to enhanced air diffusion out of the cuff. It will also

Table 2. Permeability coefficient

ml/sq cm/(cm Hg/cm) × 10^{-10}@25°C	N_2O	Air	CO_2
Material			
PVC	136	4*	72
Latex rubber	290	70	
Silicone rubber	4360	1400	

*18°C testing of new material.[2]

In the same units permeability coefficient for PVC/$O_2 \approx 12$ and for PVC/$N_2 \approx 2$.

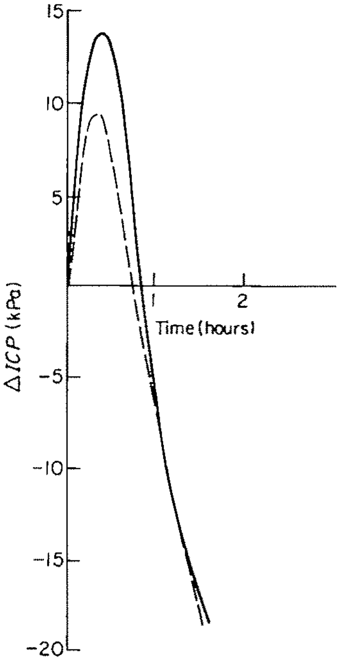


Fig. 4. Pressure changes in silicone rubber tracheal tube cuff, filled with air, in nitrous oxide. ——, Experimental; – – –, theoretical.

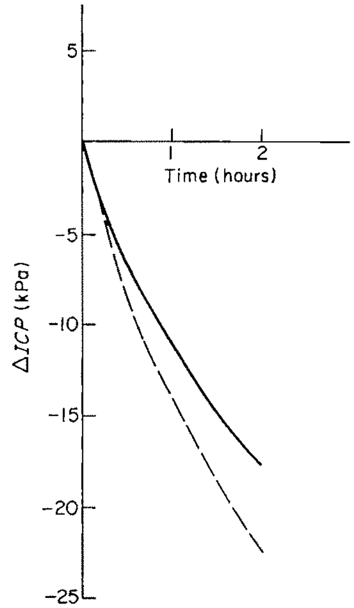


Fig. 5. Pressure changes in PVC tracheal tube cuff, filled with nitrous oxide, in nitrous oxide. ——, Experimental; – – –, theoretical.

lead to a slightly higher rate of decrease in pressure in the anaesthetic gas filled cuff. It should be noted, however, that at infinite time the intracuff pressure will be midway between the pressures above and below the cuff. If, originally, minimum leak seal is used, there will be a risk of loss of seal in time in all cases. The pressure rise may be lowered for short periods by the two methods illustrated in Figs 6 and 7. The former entails filling the cuff with carbon dioxide. This was chosen as it has a permeability coefficient approximately half that of nitrous oxide, but will permeate through both upper and lower membranes (Fig. 6).

The action of a large inflation balloon is shown in Fig. 7. The pressure rise is reduced under these circumstances. The main problem with all such systems is when a change-over from anaesthetic gas to air or air/oxygen mixtures occurs. Special attention will have to be paid to cuff pressure monitoring at these times.

The theory can thus be used to predict the behaviour of cuff systems in practice. It shows those factors which are important in determining the extent of pressure changes. Any changes in these factors can bring their own problems. It is easier to list them and see the effect brought about by such changes.

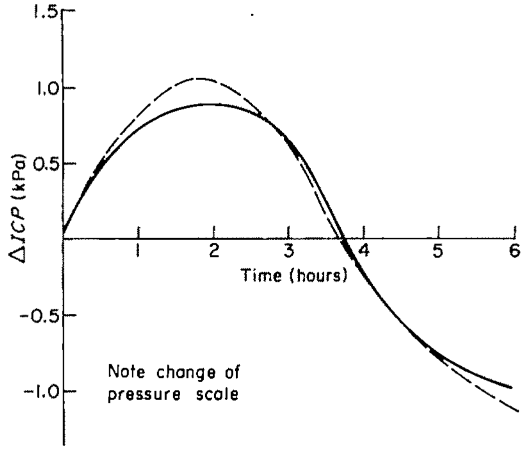


Fig. 6. Pressure changes in PVC tracheal tube cuff, filled with carbon dioxide, in nitrous oxide. ——, Experimental; ----, theoretical.

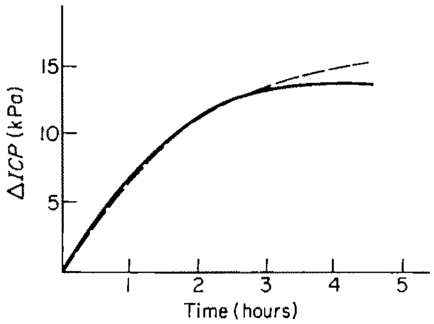


Fig. 7. Pressure changes in PVC tracheal tube cuff, with external PVC reservoir, filled with air, in nitrous oxide. ——, Experimental; ----, theoretical.

Permeability coefficient

It has been shown that the permeability to gases is related to the crystallinity, cohesive energy and cross linking of the polymer.[12] Thus, a material of high cohesive energy such as polyester (Trade Name Melinex), which is also semi crystalline, has low permeability.

It can also be readily seen, from the derived equations, that the pressure rise depends upon the relative permeation rates for the various gases involved. Thus, the pressure increase would be slower in polyester cuffs than in PVC cuffs of equal thickness. However, it would be impracticable to make polyester cuffs of such thickness as they would be too stiff and this advantage would disappear. The maximum pressure reached would also be higher. On the other hand, silicone rubber has a low cohesive energy and shows a high permeability to all gases. Cuffs made of a material of even higher permeability would deflate too easily to be practical.

Thickness

The rate of pressure increase is inversely proportional to cuff thickness—thinner cuffs show a faster pressure increase.

Volume

An increase in volume results in a lower rate of increase. This can be achieved by lengthening the cuff, which results in more damage to the trachea,[13] or by fitting an external volume reservoir,[11] which not only alters the volume but the area ratio as well. The use of an external reservoir does offer some attractions, but extra care is needed to maintain a no leak seal.

Cuff filling medium

The use of saline as a filling medium will be effective in reducing the increase in pressure. Care should be taken to eliminate all air from the system and the dynamic behaviour of the cuff system[14] is worthy of study. The suggested use of the anaesthetic gas as a cuff filling medium carries the risk of loss of seal under certain conditions, and should not be regarded as an automatic regulating system. For up to 3 hours use, a third gas (e.g. CO_2) will provide some regulation. The conditions under which the cuffs were tested did not mimic clinical practice, but do show the applicability of the derived equation.

The theory can be applied to clinical practice, however, if some assumptions are made: that the typical male and female tracheas are circular, with a diameter of 20.5 mm and 16.5 mm respectively. (The contact area is then the area of the trachea minus the cross sectional area of the tracheal tube), that the volume of the cuff is the volume of air added to make the seal and that the temperature of the cuff is about 36°C.

Using the formula, an approximate pressure rise can be calculated. This was found to give pressure rises within 10 percent of actual in a series of experiments.[3] The applicability of the theory to the *in vivo* situation can thus be assumed.

When anaesthetic gases are being considered, the method is accurate enough if air is assumed to be a single gas. However, most of the transport of gas through the membrane is that of oxygen.[4] This can become important when oxygen enriched air is used. The theoretical equation should then be used, using the partial pressures of oxygen involved.

The result is an increase in pressure rather than the gradual decrease suggested by the simplified method. During oxygen therapy, with 30 per-cent oxygen, the pressure in the cuff could increase by 0.9 kPa (90 mm H_2O) under the worst conditions.

In summary, then, it can be said that the pressure in an inflated cuff will not remain constant The pressure may rise or fall in a manner which can be predicted using the characteristics of the cuff and its dimensions. The various methods which have been suggested to overcome the pressure rise during anaesthesia should only be regarded as palliatives for the short term. Cuff pressure monitoring on a regular basis should be regarded as the ideal practice, and special attention should be given at times of change over of inspired gas.

References

1. Chandler M, Parry AM, Watson WF. Cuff pressure changes by nitrous oxide. *Proceedings of the Biological Engineering Society 20th Anniversary International Conference* 1980. London. p 491–4.
2. Chandler M. The pressure rise in tracheal tubes during anaesthesia. MSc Thesis, University of Kent at Canterbury, 1981.
3. Stanley TH, Kawamura R, Graves C. Effects of nitrous oxide on volume and pressure of endotracheal tube cuffs. *Anesthesiology* 1974; **41:** 256–62.
4. Stanley TH. Nitrous oxide and pressures and volumes of high-and low-pressure endotracheal tube cuffs in intubated patients. *Anesthesiology* 1975; **42:** 637–40.
5. Loeser EA, Orr DL, Bennett GM, Stanley TH. Endotracheal tube cuff design and postoperative sore throat. *Anesthesiology* 1976; **45:** 684–7.
6. Adriani J, Phillips M. Use of the endotracheal cuff; some data pro and con. *Anesthesiology* 1957; **18:** 1–14.
7. Dunn CR, Dunn DL, Moser KM. Determinants of tracheal injury by cuffed tracheostomy tubes. *Chest* 1974; **65:** 128–35.
8. Larsen AB. Trakeal stenose efter N_2O diffusion ind i Raleterballonen. *Ugeskrift, for Laeger*, 1979; **141:** 3520–2.
9. Patel RI, Oh TH, Epstein BS. Effects of nitrous oxide on pressure changes of tracheal tube cuffs following inflation with air and saline. *Anaesthesia* 1983; **38:** 44–6.
10. Revenäs B, Lindholm CE. Pressure and volume changes in tracheal tube cuffs during anaesthesia. *Acta Anaesthesiologica Scandinavica* 1976; **20:** 321–6.
11. Brandt L, Pokar H. Das rediffusionssytem. *Anaesthetist* 1983; **32:** 459–64.
12. Stannet V, Hopfenbert HB, Petropoulos JH. In: *Macromolecular science*. Bawn CEH, ed. London: Butterworths 1972.
13. Loeser EA, Bennett GM, Orr DL, Stanley TH. Reduction of postoperative sore throat with new endotracheal tube cuffs. *Anesthesiology* 1980; **52:** 257–9.
14. Crawley BE, Cross DE. Tracheal cuffs. *Anaesthesia* 1975; **30:** 4–11.

Appendix

Transfer of gas through a membrane occurs by permeation. The rate of permeation is determined by the permeability coefficient Q the area in contact A with the gas and the partial pressure gradient across the membrane $\frac{\Delta p}{L}$ i.e. $q = QA\frac{\Delta p}{L}$ where q is the mass transfer per unit time.

The permeability coefficient is temperature dependent. In practice, with tracheal intubation the situation presented schematically in Fig. 8 prevails. Under these conditions V = volume of cuff; p_i = partial pressure of the ith gas; a = above cuff; b = below cuff; c = inside cuff; A = surface area of cuff in contact with gas; L = thickness of cuff material; Q_i = permeability coefficient of ith gas in cuff material; ml/s/sq cm/(cmHg/cm).

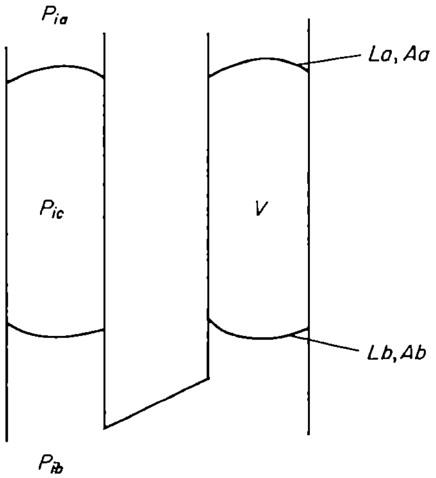


Fig. 8. Schematic diagram of cuff.

Then the total inflow of gas into cuff will be given by

$$q = \sum_{i=1}^{i=l} Q_i\left[A_b\left(\frac{p_{ib} - p_{ic}}{L_b}\right) + A_a\left(\frac{p_{ia} - p_{ic}}{L_a}\right)\right].$$

Let

$$x = \frac{A_a}{A_b} \cdot \frac{L_b}{L_a} \text{ and } p_{ix} = p_{ib} + x p_{ia},$$

then for the ith gas

$$q_i = \frac{dv}{dt} = Q_i \frac{A_b}{L_b} (p_{ix} - (1 + x) p_{ic}).$$

From the gas laws

$p_{ic} = \dfrac{n_{ic} RT}{V}$ where n_{ic} = number of moles of ith gas in cuff; R = universal gas constant; T = temperature of gas (absolute).

Then

$$dp_{ic} = \frac{dn_{ic} RT}{V},$$

but

$dn_{ic} = \dfrac{dv}{V_m}$ where V_m = molar gas volume (22.4 l.).

At N.T.P.

$\dfrac{RT}{V_m} = P_o$ = atmospheric pressure.

$$\therefore dp_{ic} = \frac{dv_{ic} T_m P_o}{V 273} \therefore \frac{dp_{ic}}{dv_{ic}} = \frac{T_m P_o}{273 V}$$

where T_m = temperature at test (absolute).

Let

$$\frac{dp_{ic}}{dt} = \frac{dV_{ic}}{dt} \cdot \frac{dp_{ic}}{dV_{ic}}$$

Then

$$\therefore \frac{dp_{ic}}{dt} = \frac{T_m Q_i A_b P_o}{273 V L_b} [p_{ix} - (1 + x) p_{ic}].$$

Let

$$K_i = \frac{T_m Q_i A_b P_o}{273 V L_b} \text{ and } p_{ico} = p_{ic}(t = 0).$$

then on integrating and rearranging, at constant temp and volume

$$p_{ic} = \frac{p_{ix} - [p_{ix} - (1 + x) p_{ico}] e^{-(1+x)K_i t}}{1 + x}.$$

Then total pressure change in the cuff.

$$\Delta p = \sum_{i=1}^{i=l} p_{ic} - \sum_{i=1}^{i=l} p_{ico}$$

When ΔP is positive, the volume of the cuff will tend to increase due to the elasticity of the material. Under the test conditions, this was confined to a slight ballooning of the ends of the cuff and hence a negligible change in volume. *In vivo*, the elastic nature of the trachea may result in a more dramatic volume change.

Anaesthesia, 1986, Volume 41, pages 294–295

The stability of preservative-free morphine in plastic syringes

R.J. BRAY, P. A. DAVIES AND J. A. SEVIOUR

Summary

The stability of preservative-free morphine in plastic syringes over 36 hours in the range of concentrations commonly used in our hospital to provide continuous morphine infusions was investigated. The morphine concentration remained at 100% (SD 1.5 percent) of the control values over 36 hours and demonstrates that the concentration of morphine is not reduced with time in these circumstances.

Key words

Analgesics; morphine.

Continuous morphine infusions have been used at the Fleming Hospital for Sick Children for a number of years.[1] Initially, morphine with preservative was used to make up the infusion solutions, but a high incidence of phlebitis at the cannula site prompted a change to preservative-free morphine. This change considerably reduced the incidence of phlebitis without seeming to alter the clinical effect of the morphine.

It was subsequently pointed out, however, that preservative-free morphine (200 μg/ml) appears to deteriorate in plastic syringes in as short a time as 20 minutes with the probable formation of apomorphine.[2,3] The infusions did not seem to lose their clinical potency, nor was there any evidence of the vomiting that might be expected if significant amounts of apomorphine were present.[4]

This study was undertaken to determine the concentrations of morphine delivered from continuous infusions of different concentrations and at different time intervals up to 36 hours.

Methods

Four 60 ml polypropylene syringes (Monoject) were filled with 50 ml of normal saline and 5, 15, 25 and 50 mg of preservative-free morphine (Macarthy's Ltd.) was added, giving approximate concentrations of 100, 300, 500 and 1000 μg/ml of morphine in normal saline. A control sample of one ml was taken, after mixing, from each syringe and stored at −18°C in a glass tube until it was assayed. The syringes were fitted into syringe pumps (Treonic IP3) and 2m of polyvinyl chloride catheter (Vygon) was attached to each of the syringes. A bacterial filter (Millex O.R.) was fitted to the end of each of the plastic catheters. Subsequent samples were taken from the outlets of the bacterial filters by temporarily increasing the rate of the syringe pump. The syringes were all kept at room temperature and set to run at 1 ml/hour. Samples were taken immediately after setting up and at 6, 12, 24 and 36 hours afterwards and were stored with the controls.

R.J. Bray, MB, BS, FFARCS, Consultant, P.A. Davies, BMSc, MB, ChB, FFARCS, Senior Registrar, Department of Anaesthesia, Royal Victoria Infirmary, Newcastle and Fleming Hospital for Sick Children, Great North Road, Newcastle upon Tyne, NE2 3AX, J.A. Seviour, BSc, FIMLS, Chief Medical Laboratory Scientific Officer, Department of Clinical Chemistry, Newcastle General Hospital, Westgate Road, Newcastle upon Tyne, NE4 6BE.

0003–2409/86/030294 + 02 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Morphine concentrations, mean of two determinations, expressed as a percentage of the control values

	Time (hours)					
Morphine (mg) added to 50 ml normal saline	Control	0	6	12	24	36
5	100	98.6	100	99.3	99.3	100
15	100	100	98.9	98.9	100	100
25	100	100	100.6	100.6	100	100
50	100	98.6	98.6	100	100	99.2

The morphine was assayed using a modification of a previously published high pressure liquid chromatographic method.[5] The chromatograph consisted of a Waters 6000A pump, a Negretti and Zambra M190 valve fitted with a 20-μlitre loop and a Waters 441 detector operating at 254 nm, coupled in series with a Pye LC-UV detector operating at 284 nm. The column was 10 cm long, had an internal diameter of 4.5 mm and was packed with 5 μ Hypersil ODS. The mobile phase consisted of 110 ml acetonitrile (Koch-Light HPLC grade), 10 ml 2% sulphuric acid (A.R. grade), 25 ml 1 percent ammonium acetate (A.R. grade), 30 ml 2 percent heptane-sulphonic acid—sodium salt (Fisons HPLC Grade), 325 ml distilled water. The solvent was degassed with helium before being pumped through the column at a rate of 1 ml/minute. Under these conditions the morphine had a retention time of 5 minutes.

Samples of 100 μlitres were used to flush and fill the 20 μlitre sample loop. The use of this procedure in conjunction with an air flush in between each sample injection ensured complete flushing and filling of the loop. All the samples were injected in duplicate and the mean result taken. The ratio of peak height at 284 mm to peak height at 254 nm was measured for each sample to monitor the peak integrity, and remained constant at 1.66. The percentage purity of the samples was expressed as the peak height at 284 nm of the sample compared with the peak height at 284 nm of the control.

Results

The results are displayed in Table 1.

Discussion

The four infusions were set up in exactly the same way as they are normally used clinically and the concentrations were all within the clinical range. The assay results up to 36 hours showed that the concentration of morphine remained within 1.5 percent of the control values, thus demonstrating that no decay of morphine had occurred in these circumstances.

In conclusion, it has been impossible to demonstrate any reduction in concentration of preservative-free morphine over a period of 36 hours in the particular circumstances of the morphine infusion used in our hospital.

References

1. BRAY RJ. Postoperative analgesia provided by morphine infusion in children. *Anaesthesia* 1983; **38:** 1075–8.
2. ORR IA, DUNDEE JW, MCBRIDE C. Preservative free morphine denatures in a plastic syringe. *Anaesthesia* 1982; **37:** 352.
3. ORR IA. Postoperative analgesia provided by intravenous morphine infusion in children (letter). *Anaesthesia* 1984; **39:** 291.
4. BRAY RJ. Postoperative analgesia provided by intravenous morphine infusion in children (letter). *Anaesthesia* 1984; **39:** 291.
5. MOORE RA, BALDWIN D, MCQUAY HJ, BULLINGHAM RES. HPLC of morphine with electrochemical detection: analysis in human plasma. *Annals of Clinical Biochemistry* 1984; **21:** 125–30.

Anaesthesia, 1986, Volume 41, pages 296–301

CASE REPORT

Anaesthesia for Friedreich's ataxia

Case report and review of the literature

C. F. BELL, J. M. KELLY AND R. S. JONES

Summary

A patient with Friedreich's ataxia was anaesthetised on two occasions. The neuromuscular blocking agent was atracurium 0.5 mg/kg on the first occasion and tubocurarine 0.5 mg/kg on the second. The effect of each was monitored using the train-of-four twitch technique. Friedreich's ataxia has been reported to cause a marked sensitivity to non-depolarising muscle relaxants and hyperkalaemia, with resulting cardiac dysrhythmias after suxamethonium. This patient did not demonstrate an abnormal response to either relaxant; the operating conditions were satisfactory and recovery was not delayed. These drugs may be safely used in this condition provided that monitoring is adequate.

Key words

Friedreich's ataxia.
Neuromuscular relaxants; atracurium, tubocurarine.

Friedreich's ataxia, although rare, is the most common of the hereditary ataxias. It is usually transmitted in an autosomal recessive manner, although sporadic cases do occur. It occurs equally in males and females. There is a progressive degeneration of the spinocerebellar and pyramidal tracts, together with dorsal root ganglion atrophy, giving rise to mixed upper and lower motor neurone involvement. The disease is usually steadily progressive, and few patients survive more than twenty years after the onset of symptoms, although it can arrest spontaneously.[1]

The main complaint is of ataxia, most marked in the lower limbs and often accompanied by dysarthria, nystagmus (present in 70%) and skeletal muscle weakness. Optic atrophy and retinal pigmentation occur and there is significant cardiomyopathy in 10–50% of these patients.[2] Pes cavus and scoliosis almost always develop. Death is often sudden and may be associated with cardiac dysrhythmias. Surgery may be required in this condition for associated problems (e.g. pes cavus or kyphoscoliosis) or for problems unrelated to the neurological disease.

There is little in the literature concerning the use of muscle relaxants during anaesthesia—only one case report from Japan,[3] in which a 47 kg boy demonstrated hypersensitivity to tubocurarine; 3.9 mg produced apnoea for 90 minutes when used with nitrous oxide, oxygen and halothane. Kadis[4] discusses management of Friedreich's ataxia under spinocerebellar de-

---

C.F. Bell, MB, ChB, FFARCS, Senior Registrar, University Department of Anaesthesia, J.M. Kelly, MB, BAONUI, FFARCS, Consultant, Royal Liverpool Hospital, Liverpool, R.S. Jones, Dr, Vet, Med, FRCVS: Senior Lecturer, University Department of Anaesthesia, Liverpool.

Correspondence to be addressed to Dr C.F. Bell, Consultant Anaesthetist, Glan Clwyd Hospital, Bodelwyddan, Clwyd, North Wales.

0003–2409/86/030296 + 06 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

generation and, although there is no specific reference to the use of muscle relaxants in this disease, he recommends that patients with Friedreich's ataxia should be managed as those with amyotrophic lateral sclerosis. Defalque and Musunuru[5] also state that anaesthesia in Friedreich's ataxia should be managed as for amyotrophic lateral sclerosis. Patients with the latter disease are vulnerable to hyperkalaemia following the administration of suxamethonium. They may also have electromyographic abnormalities and a marked sensitivity to non-depolarising muscle relaxants, as seen in cases of myasthenia gravis. Cooperman[6] reported hyperkalaemia resulting in dysrhthmias following normal doses of suxamethonium, in patients with disorders resulting in denervated muscle. In 1961, Mulder, *et al.*[7] reported marked sensitivity to a non-depolarising muscle relaxant in four patients with amyotrophic lateral sclerosis; a dose of 0.16 mg/kg produced marked muscle weakness. Thus, the problems of sensitivity both to non-depolarising muscle relaxants and hyperkalaemia following suxamethonium, together with the cardiomyopathy often seen in Friedreich's ataxia,[2] must all be considered if anaesthesia is required.

We report the details of a patient with Friedreich's ataxia, in whom neuromuscular monitoring using the train-of-four twitch response was employed throughout anaesthesia on two separate occasions using two different non-depolarising agents, atracurium and tubocurarine. A brief account of the postoperative course is included, because it may be of relevance to those interested in management of these cases.

Case history

A female, aged 16 years, was presented for a two stage correction of spinal scoliosis—a costectomy, to be followed by the definitive correction of the spinal scoliosis. She had first presented when aged 12 with a 2-year history of clumsiness of gait. There was no family history of the disease and four siblings were alive and well. A presumptive diagnosis of Friedreich's ataxia was made.

When aged 16 she attended the Royal Liverpool Hospital with a 2-year history of spinal scoliosis which had become worse in the last 3 months and she had become greatly concerned at her appearance. Apart from aching pain and some awkwardness of gait, there were no other complaints. On examination, the patient was found to look pale and weighed only 42 kg. She had a high-stepping gait and there was bilateral nystagmus and optic atrophy in the left eye. A marked thoracic scoliosis was present, with the convexity to the right and considerable posterior rib prominence on that side. The lower limbs showed wasting of the thighs and calves with bilateral pes cavus and diminished reflexes. There were no clinical signs of cardiac enlargement and no evidence of cardiac failure.

The haemoglobin was 10 g/d litre and a bone marrow analysis confirmed iron deficiency. Chest X ray showed the heart size to be at the upper limit of normal. The ECG showed non-specific T-wave inversion in leads II, III and aVF (this was not considered indicative of cardiomyopathy). Nerve conduction studies (right arm and leg) showed evidence of sensory axonal damage, but motor conductive velocities were within normal limits. Blood electrolytes, liver function tests and blood gas analysis were all within normal limits. The pulmonary function tests showed a marked restrictive abnormality, the forced vital capacity being 2.1 litres (predicted value 3.7 litres), forced expiratory volume in one second 1.8 litres (predicted 3.2 litres), the total lung capacity 3.91 litres (predicted 5.2 litres) and the residual volume 1.76 litres (predicted 1.5 litres).

First operation: costectomy

The patient was premedicated with diazepam 10 mg orally. With the patient's agreement, the equipment to monitor neuromuscular function was set up on the right arm before induction and control responses were recorded using the train-of-four twitch technique.[8] Anaesthesia was induced with fentanyl, droperidol and thiopentone. Further control twitch responses were obtained while the anaesthetised patient breathed spontaneously a mixture of nitrous oxide and oxygen. Atracurium 0.5 mg/kg was then administered via a fast flowing infusion. The train-of-four response disappeared completely at 73 seconds and tracheal intubation was carried out at 90 seconds. Intermittent positive pressure ventilation was then instituted using nitrous oxide 60% in oxygen and adjusted to provide an end-tidal carbon dioxide value of about 4.6 kPa.

Incremental doses of atracurium 0.2 mg/kg were given when the first twitch response had returned to 20% of control value; supplements of fentanyl were administered when judged clinically necessary. After 1 hour 35 minutes the anaesthetic was supplemented with enflurane 0.4–1% to induce controlled hypotension for surgery. The systolic blood pressure was maintained at 80 mmHg for 1 hour 3 minutes. The enflurane was discontinued 1 hour prior to administration of the anticholinesterase. Residual neuromuscular blockade was antagonised with neostigmine 5 mg given in two doses of 2.5 mg, 5 minutes apart at the end of surgery; each was preceded by atropine 0.6 mg. The twitch response had returned to 24% of its initial value and the patient had already started to breathe spontaneously at the time of administration of the first dose of neostigmine. Ten minutes after the second dose of neostigmine, when, clinically, there was good muscle tone, the patient was extubated uneventfully. The whole procedure lasted 4 hours, during which the patient received a total dose of atracurium of 60 mg. Recovery from this operation was completely uneventful, with no detectable change in neurological signs or symptoms.

Second operation: Harrington rod instrumentation. T_4-L_2

Fourteen days after her costectomy the patient was anaesthetised again. In order to compare the relative merits of the two relaxants, tubocurarine was used on this occasion and the procedure was otherwise as before. The initial dose of tubocurarine was 20 mg (0.5 mg/kg); intubation was performed easily 130 seconds after this, even though the initial twitch height had not declined at all. Maximum depression of the first twitch (to 20% of control) was reached 14 minutes after the initial dose had been given.

Increments of tubocurarine 0.1 mg/kg were given when the first twitch response had returned to 20% of control height. Enflurane 0.6–2% was added to produce controlled hypotension, with a systolic blood pressure of 80–100 mmHg. It was commenced 2 hours 20 minutes after induction, continued for 3 hours and discontinued 40 minutes before the end of the procedure. The operation lasted 6 hours 40 minutes and in this time the patient received 50 mg tubocurarine.

Reversal of the neuromuscular block (with two doses of neostigmine 2.5 mg) as before, was rapid and complete. The first twitch response had returned to 57% when the first dose of neostigmine was given. Recovery from anaesthesia again was uneventful; the patient awakened quickly and was able to move all four limbs.

Subsequent course

The first 13 days postoperatively, the patient was nursed in a hyperextended position on a plaster bed, during which time she had daily physiotherapy with a full range of movements to all limbs. On the first day she developed signs and symptoms of the superior mesenteric artery syndrome[9] which required treatment for 2 days. This presents as high intestinal obstruction caused by the narrowing of the angle between the superior mesenteric artery and the aorta; this follows correction of the spinal curve, which obstructs the third part of the duodenum.

On the fourteenth day she was put into a full plaster cast and encouraged to walk. Mobilisation was slow and difficult and even 28 days postoperatively she was only able to walk 10 m. Thirty-four days postoperatively she complained of sudden onset of upper chest pain and shortness of breath, and was found to have tachycardia with a gallop rhythm and hypotension. Chest X-ray was unremarkable and the ECG showed a sinus tachycardia with occasional ventricular ectopics. Pulmonary embolus was diagnosed and anticoagulation with heparin was commenced. The following day her condition had deteriorated further and a flow-directed pulmonary artery catheter was inserted (to aid diagnosis and permit thrombolytic therapy into the pulmonary artery). The pulmonary wedge pressure was found to be high (20 mmHg) and the cardiac output low (1.3 litres/minute). However, lung scan and angiography both failed to show evidence of embolism. There were some signs of myocardial infarction on the ECG, and the cardiac enzymes were raised.

Despite supportive therapy with dopamine and positive pressure ventilation, the patient died on the thirty-eighth day after surgery. At postmortem there was gross pulmonary oedema together with a small amount of antemortem thrombus in the peripheral vessels of both lungs. No source of thrombus was found. The heart was moderately enlarged, with left ventricular hypertrophy and some degree of obstruction. Following the postmortem findings, it was concluded that the relatively small pulmonary emboli present in the periphery of the lungs were sufficient, in this patient, to cause acute cardiac

Table 1. Times of incremental doses from time of intubation in minutes

	Atracurium			Tubocurarine		
Increment	F.A.	Normal	(SD)	F.A.	Normal	(SD)
1st	34	43	(11.2)	35	44.7	(15.2)
2nd	56	71	(19.6)	77	55.7	(21.8)
3rd	97	89	(21)	113	83.0	(22.6)
	—			—		
4th	148	99	(40.3)	188		
5th	186	129	(72.4)	251		
6th	—	218				

Normal values with standard deviation (SD).[10] F.A.—Friedreich's ataxia. After the third increment for the patient with FA, enflurane was added, so direct comparison is no longer possible with the normal series.[10]

failure in the presence of long-standing hypertrophic cardiomyopathy.

Results of neuromuscular monitoring

The mechanical response to the train-of-four stimuli was recorded using a force displacement transducer (Grass FT 03C) and pen recorder. A normal train-of-four response (no fade) was obtained in control tracings on both occasions. The results obtained were compared with findings reported in normal patients studied in the same way.[8,10] Following the initial dose of atracurium, the time to disappearance of the first twitch of the train-of-four (73 seconds in the patient with Friedreich's ataxia) was similar to the time found in normal patients (mean 110, SD 28). Following the initial dose of tubocurarine in this patient, the first twitch response did not disappear completely, but reached maximum depression at 13 minutes. A similar response is found in some normal patients, although in these patients the mean time to maximum depression was shorter (mean 4 minutes, SD 3).

In the patient with Friedreich's ataxia, the time to 20% recovery of the initial twitch height following atracurium was somewhat faster, at 34 minutes, than for normal patients in whom the mean time was 43 minutes (SD 11). The time to 20% recovery after tubocurarine in the patient with Friedreich's ataxia was 35 minutes, compared to a mean time in normal patients of 45 minutes (SD 15).

Increment times are given in Table 1. It can be seen that the times at which each increment was given before enflurane was added are comparable with the results obtained from normal patients. Clinically acceptable reversal of the residual neuromuscular blockade was obtained in the patient with Friedreich's ataxia after neostigmine 5 mg following each of the muscle relaxants. The height of the initial twitch had returned to 65% after neostigmine following atracurium, and to 142% after neostigmine following tubocurarine.

Discussion

Defalque and Musunuru[5] and Kadis[4] have all pointed out that, as far as general anaesthesia is concerned, patients with Friedreich's ataxia share many features with patients who have amyotrophic lateral sclerosis (ALS). Patients with ALS are reported to show electromyographic evidence of a nerve conduction defect resembling myasthenia gravis in a severely affected muscle,[11,12] whilst the nerve conduction to unaffected muscle groups in the upper limbs can be within normal limits. Hence the usual neuromuscular monitoring techniques may not reveal any pathology. During electromyographic studies of the affected musculature, the evoked potentials produced by supramaximal nerve stimulation showed a progressive decline in amplitude.[7] It was also shown that four patients with ALS who had some signs and symptoms comparable with myasthenia gravis, had the strength in the affected muscles increased appreciably after neostigmine or edrophonium. They were all very sensitive to small doses of tubocurarine (requiring approximately 0.016–0.032 mg/kg).

Abnormal sensitivity in ALS to another non-depolarising muscle relaxant, gallamine, was reported by Rosenbaum, Neigh and Strobel in 1971.[13] Because of these reports, we considered it a wise precaution to monitor neuromuscular transmission throughout anaesthesia in this patient with Friedreich's ataxia, who required a non-depolarising muscle relaxant.

In the patient reported here, the control trace showed no evidence of fade as seen in myasthenia gravis, and there was no measurable abnormal response to train-of-four stimuli after normal doses of either atracurium or tubocurarine. The only suggestion of a myasthenic characteristic was seen following the reversal of the residual neuromuscular blockade produced by tubocurarine; the height of the initial twitch response was increased to 42% above the control value, whilst the ratio of the fourth twitch response to the first at this point was 85%. This effect has been reported in a series of patients with myasthenia gravis after neuromuscular blockade with atracurium was reversed by neostigmine.[14] Clinically, the patient with Friedreich's ataxia made a good recovery from the neuromuscular blockade produced by each relaxant, and the quoted hypersensitivity to tubocurarine was not manifest.

Careful clinical monitoring to ensure adequate respiratory function must be continued postoperatively; in this disease, the response of the thoracic and abdominal muscles may differ from limb musculature and this may become apparent at this stage. Even in normal patients, there is a different sensitivity to the non-depolarising muscle relaxants. Unna and Pelikan[15] found that, in normal patients, doses of tubocurarine which produced a 95% decrease in grip strength resulted in depression of vital capacity of less than 20%. Although it would be preferable to carry out simultaneous monitoring of the abnormal leg muscles or the intercostal muscles, as described by Wright and Drummond,[16] this may be clinically impracticable if it restricts surgical access.

We do not consider that either of the anaesthetics that the patient we studied received, contributed to neurological deterioration or her subsequent death. Postoperative anticoagulant therapy to reduce the risk of deep vein thrombosis may possibly have prevented the pulmonary emboli, but this is not routinely undertaken in this unit for spinal surgery.

It is recommended[4,5] that cases of Friedreich's ataxia should be treated like patients with ALS, but careful monitoring of the patient we studied showed no significant sensitivity to the non-depolarising muscle relaxants which were used. Atracurium may be clinically more predictable in such cases because of its reliable degradation by Hofmann elimination, but neuromuscular function should be monitored throughout anaesthesia.

Acknowledgments

We should like to express our thanks to Dr N. Coulshed for advice concerning the cardiology of Friedreich's ataxia, and to Professor J.E. Utting and Dr J.M. Hunter for assistance in preparation of this manuscript. We are also grateful to Professor R. Owen for allowing us to study his patient.

References

1. Walton JM. *Brain's diseases of the nervous system*, 8th edn. Oxford: Oxford University Press, 1977; 672–4.
2. Oakley C. *Oxford textbook of medicine*. Weatherall DJ, Ledingham JGG, Warrell DA, eds. 13. 195.
3. Kume M, Zin T, Oyama T. Anesthetic experience with a patient with Friedreich's ataxia—a case report. *Japanese Journal of Anesthesiology* 1976; **25**: 877–80.
4. Kadis LB. *Anesthesia and uncommon diseases*, 2nd edn. Katz J, Benumof J, Kadis LB, eds. Philadelphia: W.B. Saunders and co 1981. 492–3.
5. Defalque RJ, Musunuru VS. *Anesthesia and coexisting disease*. Stoelting RK, Dierdorf SF, Eds. Churchill Livingstone, 277.
6. Cooperman LH. Succinylcholine induced hyperkalemia in neuromuscular disease. *Journal of the American Medical Association* 1970; **213**: 1867–71.
7. Mulder DW, Lambert EH, Eaton LM. Myasthenic syndrome in patients with amyotrophic lateral sclerosis. *Neurology* 1959; **9**: 627–31.
8. Hunter JM, Jones RS, Utting JE. Use of atracurium during general surgery monitored by the train of four stimuli. *British Journal of Anaesthesia* 1982; **54**: 1243–50.
9. Rothman RH, Simeone FA. *The spine*, Vol. 1. Philadelphia: W.B. Saunders and Co, 1982: 427.
10. Hunter JM, Jones RS, Utting JE. Comparison of vecuronium, atracurium and tubocurarine in normal patients and in patients with no renal fuction. *British Journal of Anaesthesia* 1984; **56**: 941–51.
11. Lambert EH, Mulder DW. Electromyographic studies in amyotrophic lateral sclerosis. *Proceedings of the Staff Meetings of the Mayo Clinics* 1957; **32**: 441–6.
12. Rooke ED, Mulder DW, Eaton LM, Lambert EH. Studies of neuromuscular conduction in myasthenia gravis and related disorders. *Myasthenia gravis. Second International Symposium Proceed-*

ings, 1961. Springfield: C.C. Thomas; 435–43.

13. Rosenbaum KJ, Neigh JT, Strobel GE. Sensitivity to non-depolarising muscle relaxants in amyotrophic lateral sclerosis: Report of two cases. *Anesthesiology* 1971; **35**: 638–41.
14. Bell CF, Florence AM, Hunter JM, Jones RS, Utting JE. Atracurium in the myasthenic patient. *Anaesthesia* 1984; **39**: 961–8.
15. Unna KR, Pelikan EW. Evaluation of curarizing drugs in man. Critique of experiments on unanaesthetized subjects. *Annals of the New York Academy of Sciences* 1951; **54**: 480–90.
16. Wright ADG. Drummond GB. A technique for comparison of two muscle sites during neuromuscular block. *British Journal of Anaesthesia* 1983; **55**: 1164P.

Anaesthesia, 1986, Volume 41, pages 302–305

APPARATUS

The Nellcor N-101 pulse oximeter

A clinical evaluation in anaesthesia and intensive care

J. A. TYTLER AND H. F. SEELEY

Summary

The accuracy of the Nellcor N-101 pulse oximeter has been evaluated in adult patients receiving general anaesthesia or intensive care. Readings obtained noninvasively with this instrument were compared with measurements made on arterial blood using a Radiometer OSM2 oximeter. The pulse oximeter was easy to use and within the range tested (70–100 percent saturation of haemoglobin with oxygen) the readings were within 1 digit of the values obtained by in vitro *measurement.*

Key words

Oxygen; blood levels.
Measurement techniques; pulse oximetry.

The measurement of $P\text{O}_2$, now the standard means of assessing arterial oxygenation, suffers from two disadvantages. First, it is invasive and requires arterial cannulation or repeated arterial puncture. Second, unless sophisticated apparatus is used, the information provided is intermittent and only available after a delay of at least one minute.

For many purposes, arterial oxygenation can be assessed adequately by measuring oxygen saturation of haemoglobin. The Hewlett-Packard 47201A ear-oximeter has been available for over 10 years for the noninvasive determination of arterial oxygen saturation. This instrument was used in two studies recently published,[1,2] but is no longer being manufactured.

The latest generation of oximeters, the pulse oximeter, has been available in the United States for 2 years. The accuracy of one such instrument, the Nellcor pulse oximeter, has been assessed in paediatric patients[3] and in fit volunteers breathing hypoxic mixtures.[4] The present study assesses its accuracy in patients receiving general anaesthesia and intensive care.

Apparatus

The instrument measures the oxygen saturation of arterial blood in the finger pulp. A sensor is attached to the finger with adhesive tape. Within the sensor are two light-emitting diodes (LED), which transilluminate the finger with light of wavelengths 660 and 940 nm, and a photodetector. The LEDs emit alternately, so that only one photodetector is needed and no filters are necessary.

The use of two wavelengths enables the oxygen saturation of haemoglobin in the light path to be determined. However, the finger pulp contains arterial, capillary and venous blood. The signal from the photodetector is fed to a microprocessor so that only pulsatile signals are used to cal-

---

J.A. Tytler, MB, ChB, DCH, DRCOG, FFARCS, Registrar, H.F. Seeley, MSc, MB, BS, FFARCS, Consultant, Department of Anaesthetics, St George's Hospital, London SW17 0QT.
Correspondence should be addressed to H.F. Seeley please.

0003–2409/86/030302 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

culate saturation. Arterialisation by heating or chemical vasodilatation is therefore unnecessary. The sensors are sterile when delivered and are classified as for single use; however, they can be re-used and only three sensors were used during this study.

The microprocessor is contained within a display unit which gives a digital readout of saturation and pulse rate. The pulse amplitude is indicated by the vertical height of a 16 segment LED array. Displayed saturation and pulse rate are based on the mean values of the preceding 5–7 beats. Variable alarms are provided for warning of low saturation and high and low pulse rates. An internal battery is fitted. Each pulse can be accompanied by a bleep, the pitch of which varies with the saturation value, thus providing immediate auditory warning of changes in heart rate and saturation.

The unit is ready for use 15–20 seconds after switching on and stable readings are obtained after a few heart beats. Calibration is automatic. The necessary information is contained within each sensor and is read by the microprocessor. Any adjustment necessary is then carried out internally.

A chart recorder designed to accompany the pulse oximeter is available. Two chart speeds of 5 and 25 mm/minute are provided. Information is transferred to the recorder through a flexible fibreoptic link.

Methods

The study was approved by the Wandsworth District Ethical Committee. Two groups of patients participated in the study. One group was receiving treatment in an intensive care unit, the other was undergoing thoracotomy. This operation was chosen because even with impeccable anaesthetic technique, there is an incidence of arterial hypoxaemia during one lung anaesthesia. The patients' ages ranged from third to eighth decades and some patients had deeply pigmented skin. In all cases a radial artery cannula had already been inserted as part of routine management.

The pulse oximeter sensor was attached to a finger of the hand supplied by the cannulated artery. When the reading was stable, 0.25 ml of arterial blood was withdrawn and the oxygen saturation measured using an automated oximeter (Radiometer OSM2). The pulse oximeter reading was noted at the time of sampling. No more than 2 ml of blood was taken from any one patient in this study.

The performance of the OSM2 oximeter has been evaluated by Saloojee and colleagues.[7] Over the entire range of oxygen saturation (0–100 percent), measurements made by this instrument were in close linear relationship to those made by an absolute method of oxygen content analysis (correlation coefficient = 0.999; standard error of estimate = 1.5 percent O_2 saturation). The repeatability standard deviation was 0.47 percent oxygen saturation.

Results

Seventy-two paired estimates of arterial saturation were obtained. The data from the two groups of patients have been pooled and are displayed graphically in Fig. 1.

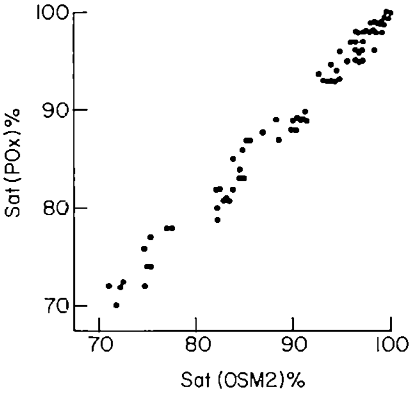


Fig. 1. Saturations measured by OSM2 oximeter (Sat (OSM2)%) plotted against saturations measured by Nellcor pulse oximeter (Sat(POx)%).

The data have been analysed by the method suggested by Altman and Bland[5] for the comparison of two methods of measuring the same quantity. The differences between pairs of measurements are studied: a histogram of differences gives an indication of the statistical distribution; a plot of differences against the mean values permits an assessment of error and bias throughout the range studied. A paired *t*-test on the mean of observed differences as compared with a mean of zero gives a value to the probability of inherent bias in one method as compared with standard.

The results are presented in Table 1. They

Table 1. Summary of statistics on differences between pairs of saturation measurements

Sat (OSM2)%–Sat (POx)%	
Number	72
Range	2.3% to −2.5%
Mean	0.4%
Standard deviation	1.2%
S.E. mean	0.1%
95% confidence interval for mean	0.1% to 0.7%
Paired *t*-test on differences, mean = 0	p = 0.005

indicate that the pulse oximeter tends to under-read slightly when compared with the OSM2, the mean difference being 0.4 percent O_2 saturation. This could in part be due to truncation by the Nellcor instrument; for example, saturations between 94.0 and 94.9 percent would be displayed as 94 percent. The results are well within the manufacturer's specification of 2 digits within the range 70–100 percent saturation.

Discussion

A recent review of methods for monitoring oxygenation during anaesthesia suggested that 'reliance on clinical observation to detect hypoxaemia would seem to be at best unwise'.[6] It also suggested that pulse oximetry is becoming 'care-standard' for anaesthetic practice in the United States.

The adoption of this technique during routine anaesthesia seems unlikely in the United Kingdom, but there are occasions when rapid warning of a decrease in arterial saturation would be very useful. Hypoxaemia frequently accompanies bronchoscopy, dental chair and thoracic anaesthesia, and pulse oximetry would be a valuable guide to arterial oxygenation during high frequency ventilation. It would also indicate hypoxaemia during tracheal suction and chest physiotherapy.

Both oximeters used in this study are designed to measure functional haemoglobin saturation. By definition, this saturation is unaffected by the presence of other haemoglobin species such as carboxyhaemoglobin; this substance may, however, interfere with the measurement. The OSM2 is so designed that carboxyhaemoglobin has a negligible effect when the saturation is within the physiological range; for the Nellcor instrument, the maximum measurement error is 10 percent of the carboxyhaemoglobin percentage[4] and, for clinical purposes, this error can be ignored. However, the presence of other coloured substances, such as methaemoglobin, bilirubin or Cardiogreen, may affect the accuracy.

In this study, the pulse oximeter was not tested in patients who were severely hypotensive or hypothermic, nor has the accuracy been determined when arterial saturation is below 70 percent. Under standard conditions a saturation of 70 percent corresponds to a $P\text{O}_2$ of about 5 kPa, and such low values are rarely encountered in arterial blood.

The Nellcor pulse oximeter is easy to use and provides, noninvasively, a rapid and accurate indication of arterial oxygen haemoglobin saturation. It would benefit from provision of electrical outputs, so that saturation and heart rate could be recorded on other chart recorders. The Nellcor Recorder lacks an event marker, and a much wider range of chart speeds would increase its versatility.

Manufacturers

The Nellcor N-101 pulse oximeter and Nellcor N-9000 recorder are manufactured by Nellcor Incorporated, 3116 Diablo Avenue, Hayward, California 94545; the current prices (May 1985) are U.S. $5800 and U.S. $1695 respectively. Nellcor expect to market these instruments in the United Kingdom in late summer, 1985.

Acknowledgments

The authors wish to thank their consultant colleagues in the Wandsworth Health District for permission to study patients under their care and acknowledge with gratitude the statistical assistance of Dr J.M. Bland and the technical assistance of Mr I. Eversden, and of Dr T.G. Williams, Department of Clinical Measurement, Westminister Hospital, London SW1. They also wish to thank Nellcor Incorporated for the loan of the pulse oximeter and recorder.

References

1. Drummond GB, Park GR. Arterial oxygen saturation before intubation of the trachea. An assessment of oxygenation techniques. *British Journal of Anaesthesia* 1984; **56**: 987–93.
2. Jones JG. Pulmonary complications following general anaesthesia. In: Kaufman L, ed. *Anaesthesia: Review 2*. Edinburgh: Churchill Livingstone, 1984: 21–38.
3. Swedlow DB, Stern S. Continuous non-invasive

oxygen saturation monitoring in children with a new pulse-oximeter. *Critical Care Medicine* 1983; **11:** 228.

4. YELDERMAN M, NEW W. Evaluation of pulse oximetry. *Anesthesiology* 1983; **59:** 349–52.
5. ALTMAN DG, BLAND JM. Measurement in medicine: the analysis of method comparison studies. *Statistician* 1983; **32:** 307–17.
6. HANNING CD. 'He looks a little blue down this end'. Monitoring oxygenation during anaesthesia. *Britis Journal of Anaesthesia* 1985; **57:** 359–60.
7. SALOOJEE Y, COLE PV, ADAMS L. The evaluation c a photometer (the Radiometer OSM2) for th determination of haemoglobin concentration an per cent oxyhaemoglobin and carboxyhaemoglobi in blood. *Journal of Medical Engineering an Technology* 1981; **5:** 298–300.

Anaesthesia, 1986, Volume 41, pages 306–308

APPARATUS

Force exerted by epidural catheters

P. A. J. HARDY

Summary

In a study of epidural catheters, it was found that catheter material and catheter diameter both influenced the force exerted. Catheters made of nylon exert less force than those made of polyethylene. Diameter is proportional to the logarithm of force exerted.

Key words

Equipment; epidural catheters.

The abnormal placement of an epidural catheter passed through a successfully placed epidural needle has an incidence of up to 10 percent.[1] Intravenous insertion is the most frequent abnormal site, although subdural[2] or subarachnoid[3] location may occur. Correct siting of the catheter may be improved by procedures such as fluid loading the space prior to insertion.[4] The force exerted by catheter tips has been acknowledged as a factor in abnormal placement,[5] although no data exist to substantiate this.

A study was performed to assess the force exerted by catheter tips and to assess factors which may lead to a reduction in this force.

Method

A variety of epidural catheters were used (Table 1), which included all those which were readily available in the Edinburgh group of hospitals. In addition, examples of the Arrow Racz catheters were obtained and included in the analysis. Five of each type were tested.

Table 1. Catheters tested

Make	Type	Gauge	Material
Portex	Open end	16	Nylon
	Single lateral eye	16	
	Three helical eye	16	
	Three helical eye	18	
Vygon	Open end	19	Polyethylene
	Open end (Stillette removed)	19	
Arrow	Racz	20	Nylon reinforced wire

The method used was as follows. A modified Tuohy needle, with the tip removed, was used as a guide to support each catheter. The terminal 0.5 cm of catheter extended beyond the end of this guide. This length was chosen to allow flexion of the tip while remaining free of the lateral apertures in the lateral eye catheters. The catheter tip was directed perpendicularly to the pan of a Salter (No. 512) spring balance, the calibration of which had been checked prior

---

P.A.J. Hardy, BSc (Hons), MB, ChB, FFARCS, Registrar, Department of Anaesthesia, Royal Infirmary of Edinburgh, Lauriston Place, Edinburgh EH3 9YW.

Present address: Department of Anaesthesia and Intensive Care, University Hospital of Uppsala, S-751 85 Uppsala, Sweden.

0003–2409/86/030306 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

to use; the end point was taken when the catheter bent. Measurements were made at room temperature. The maximal force exerted was measured in Newtons.

Results

The results obtained were analysed by Mann-Whitney U Tests between each of the pairings (Table 2). It was found that there was no significant difference between the results for any of the 16-gauge Portex catheters or between these and the 19-gauge Vygon catheters. There was a significant reduction in force exerted by the 18-gauge Portex compared to both the 16-gauge Portex and 19-gauge Vygon types. The Arrow catheters exerted significantly less force than any of the other types tested.

Table 2. Mean force exerted (SD)

Type		Force (N)	Significance
Portex	OE	0.912 (0.027)	
	SLE	0.902 (0.027)	
	16g THE	0.912 (0.027)	
	18g THE	0.520 (0.027)	$p < 0.01$
Vygon	OE	0.961 (0.027)	
	OE	0.912 (0.027)	
Arrow		0.176 (0.027)	$p < 0.01$

OE, open end; SLE, single lateral eye; THE, three helical eye.

Discussion

In a study of the stiffness of central venous cannulae, Stenqvist and colleagues[6] identified cannula material as a major source of variation. They found that silicone elastomer, polyvinylchloride and polyurethane were much less stiff than polyethylene and teflon cannulae. They also observed that in the polyethylene group, narrower cannulae were less stiff.

In the present study, it was found that the 19-gauge polyethylene catheters exerted significantly more force than the 18-gauge nylon types. The 19-gauge polyethylene catheters exerted as much force as the larger 16-gauge nylon catheters. This supports the observation of Stenqvist *et al.*[6] that polyethylene is a more rigid material.

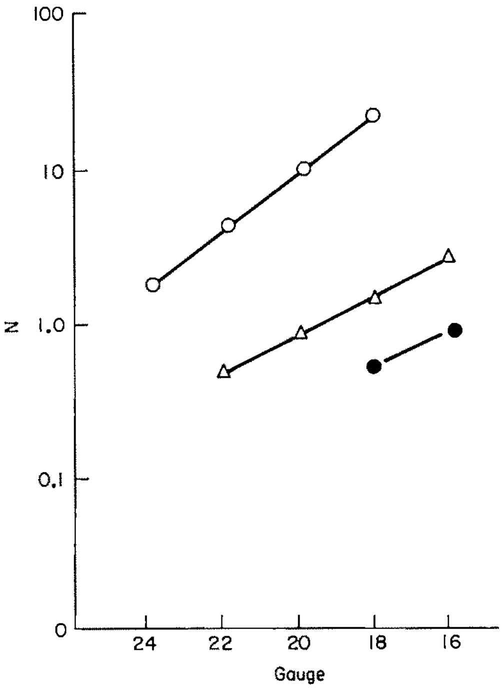


Fig. 1. The relationship between radius (r) and force exerted (F) for epidural catheters, venous cannulae and spinal needles. $r \alpha \log_{10} F$. (○), B–D spinal needles; (△), Venflow cannulae; (●), epidural catheters.

The force exerted was found to be related to diameter in the group of nylon catheters. In a series of observations on teflon venous cannulae and steel spinal needles (Hardy, unpublished data) diameter was found to be proportional to the logarithm of the exerted force (Fig. 1). Catheter diameter is therefore an important factor in tip force. The introduction of a wire-spiralled tip, as in the Arrow catheter, produces a significant reduction in exerted force. The change in design is, however, accompanied by a significant increase in cost.

In summary, the force exerted by epidural catheter tips is an acknowledged cause of abnormal catheter placement. It was found that those made of nylon exert less force than those of polyethylene. It was also found that catheter diameter is proportional to the logarithm of force exerted.

References

1. Crawford JS. *Principles and practise of obstetric anaesthesia*, 4th edn. Oxford: Blackwell Scientific Publications, 1978.
2. Boys JE, Norman PF. Accidental subdural analgesia: a case report, possible clinical implications and relevance to "massive extradurals". *British Journal of Anaesthesia* 1975; **47:** 1111–3.
3. Philip JH, Brown WU. Total spinal anesthesia late in the course of obstetric bupivacaine epidural block. *Anesthesiology* 1976; **44:** 340–1.
4. Verniquet, AJW. Vessel puncture with epidural catheters. Experience in obstetric cases. *Anaesthesia* (1980) **35:** 660–2.
5. Scott DB, Wilson J. Insertion of epidural catheters. *Anesthesia* 1983; **38:** 1108–9.
6. Stenqvist O, Curelaru I, Linder L-E, Gustavsson B. Stiffness of central venous catheters. *Acta Anaesthesiologica Scandinavica* 1983; **27:** 153–7.

Anaesthesia, 1986, Volume 41, pages 309–315

APPARATUS

Halothane and trichloroethylene

Two agents in a single vaporizer

N. HOLLIS

Summary

The vapour pressures of static mixtures of halothane and trichloroethylene and the output of th vapours from an Oxford Miniature Vaporizer filled with mixtures of the two liquids have been studi a small pilot study, a mixture of halothane and trichloroethylene was used for drawover anaesthe patients having minor surgery; this seems to work satisfactorily and may have some limited applica

Key words

Anaesthetics, volatile; halothane, trichloroethylene.
Equipment; vaporizers.

There is no single inhalational anaesthetic agent which is ideal for a patient breathing spontaneously, using only air or oxygen enriched air as the carrier gas, as would be used in a drawover anaesthetic system. Ether is flammable and induction and recovery are slow; halothane can be given until a patient is almost apnoeic and yet he may still move in response to surgical stimulus; enflurane may be better in this respect[1] and trichloroethylene alone is unsuitable for general anaesthesia without the use of muscle relaxants.

Various combinations have been used to overcome the disadvantages of individual agents and that of halothane and trichloroethylene used with oxygen enriched air has retained popularity. This was first described by Gabbe and Ozorio;[2] it has been used extensively and has been found to be clinically most useful as a drawover anaesthetic for spontaneously breathing patients.[3] The pharmacology of the two agents makes their combined use co mentary and the disadvantages of each reduced, e.g. hypnosis versus analgesia spiratory depression versus tachypnoea. Th anaesthetics are usually administered with vaporizers in series, one for halothane and o trichloroethylene, as for example in the Trisc equipment, where the two Oxford Mini Vaporizers (OMV) are used.[4]

The purpose of this study was to examin feasibility of mixing halothane and trich ethylene for draw over anaesthesia with a s vaporizer. This involved the following cedures: examination of the vapour pres above various mixtures of halothane trichloroethylene and determination of wh or not an azeotropic mixture is formed; mea ment of the vapour output from an OMV v has been filled with mixtures of the two ag use of a 3:1 mixture of halothane and trich

---

N. Hollis, MB, BS, FFARCS, Locum Senior Registrar, Magill Department of Anaesthetics, Westminster Ho Page Street, London SW1 2AP.

Correspondence should be addressed to Dr N. Hollis, 3 Hamilton Drive, Melton Mowbray, Leiceste LE13 0QY please.

0003–2409/86/030309 + 07 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

ethylene for draw-over anaesthesia with a single vaporizer to determine its usefulness as a general anaesthetic for minor surgery in spontaneously breathing patients.

Halothane–trichloroethylene liquid–vapour composition analysis

Apparatus and method

Halothane and trichloroethylene vapour pressures were measured from 20-ml glass syringes sealed with nylon stopcocks. The temperature of the liquid and vapour in the syringes was stabilised by placing them in a bucket of water at 20°C. The measurement of halothane and trichloroethylene partial pressures was made with a Centronic 200 MGA Mass Spectrometer.

Samples of 5 ml of liquid halothane and trichloroethylene mixtures were made up in sealed 20-ml syringes with 10 ml of air. Eleven different proportions were tested from pure halothane to pure trichloroethylene. The mixtures were shaken and allowed to settle for a few minutes before the atmosphere above the liquid was sampled in the mass spectrometer. Each proportion of the mixture was made up ten times and each was sampled. The temperature was maintained at 20°C by a water bath and the pressure within the syringe was allowed to equalise with that outside (101.6 kPa).

Calibration of the mass spectrometer. It was found that by shaking 5 ml of halothane or trichloroethylene in a sealed 20-ml glass syringe with 10 ml of air, a saturated vapour could consistently be produced. This was verified by checking the predicted vapour strengths against that measured in a Raleigh refractometer (in the case of halothane the sample was diluted 10:1 with air before reading). The saturated vapours made in the syringes were used to calibrate the mass spectrometer in the high concentration ranges being looked at (33% halothane and 9% trichloroethylene).

No formal test of the linearity of the digital voltmeter output was made. In low concentration ranges (0–6% halothane), the accuracy of the digital voltmeter was confirmed using independent standards of known vapour strengths provided by British Oxygen Company (BOC) or made by dilution of known quantities of halothane and trichloroethylene. The calculated vapour concentrations were verified by refractometry. In the high concentration range, vapours were made up at temperatures between 19 and 22°C, i.e. saturated concentrations of halothane 31–35%, but the mass spectrometer nevertheless read consistently for the agents measured at 20°C from the syringe in the water baths.

Results

These are shown in Fig. 1. The symbol · represents each different liquid proportion of halothane and trichloroethylene studied. The position of the symbol on the x axis represents the mole fraction of halothane in trichloroethylene in the liquid. The position on the y axis represents the combined partial pressures of halothane and trichloroethylene in the mixture. The bar represents one standard deviation each side of the mean (there were ten readings in each case). Each group of samples is linked by equilibrium tie-lines to 0, which show the proportions of the two agents in the vapour phase at a common total pressure.

Vapour output

Apparatus and method

The equipment is shown diagrammatically in Fig. 2. The vaporizer used was an OMV 50. The settings were graded in terms of angular scale settings: at 0° the vaporizer is off, at 20° the ports begin to open and at 80° the output is maximal. The vaporizer was connected by rubber elephant tubing to a Starling respiration pump, which drew air through the vaporizer in a fashion to mimic normal breathing; thus, a volume of 350 ml was drawn through fifteen times a minute, giving a minute volume of 5.2 litre/minute. The vapour concentrations produced by the OMV were measured by a Centronic 200 MGA mass spectrometer. This was calibrated with a mixture of 2% halothane and 1% trichloroethylene, provided by BOC.

The OMV was filled with 50 ml of halothane and trichloroethylene mixture. Three proportions of the two agents were examined: 37.5 ml halothane and 12.5 ml trichloroethylene (3:1); 30 ml halothane and 20 ml trichloroethylene (3:2) and 25 ml of each (1:1). Outputs of the vapour were measured at various settings for the 3:1 mixture (the one that was reckoned to be the most useful for clinical use). Between measurements at each setting (30°, 40°, 50°, 60°, 70°, 80°), the vaporizer was emptied of any unused liquid and refilled with fresh mixture. The output was initially

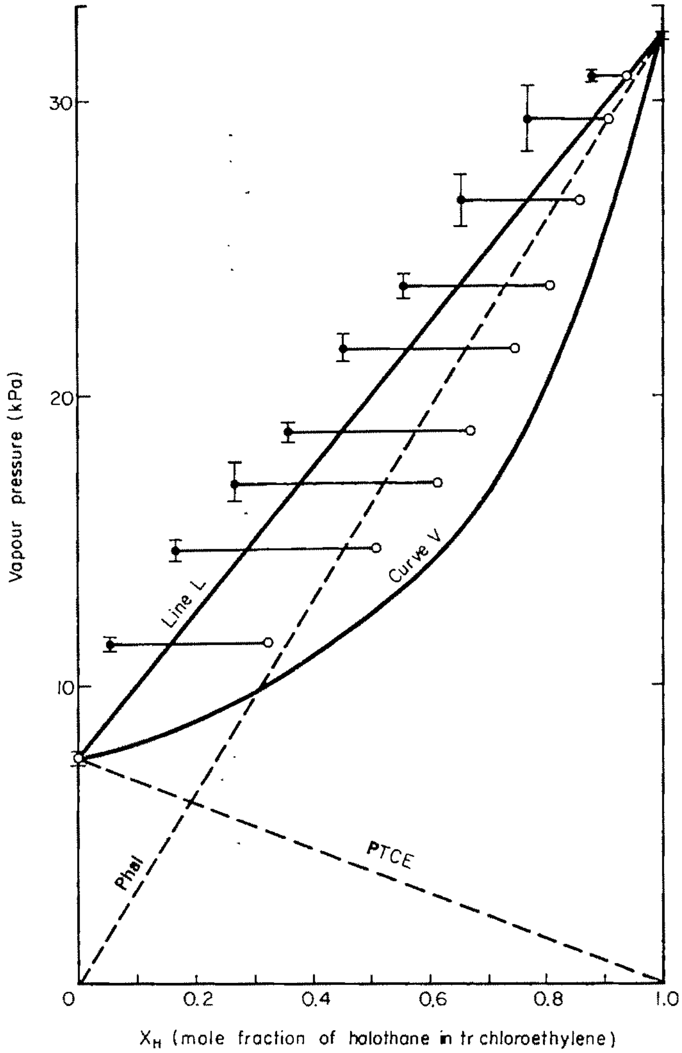


Fig. 1. Vapour-pressure composition diagrams for halothane and trichloroethylene. Temperature 20°C at 101.6 kPa atmospheric pressure. Phal and P_{TCE} represent the partial pressure of halothane (H) and trichloroethylene (TCE) in the liquid phase; line L is their sum. Curve V gives the corresponding vapour composition with the liquid at a certain pressure. These are calculated for H and TCE, assuming they behave as an ideal liquid pair and obey Raoult's Law. (Ɨ) Represents the liquid composition and vapour pressure found by experiment (mean/,SD). These points are joined by equilibrium tie-lines to points ○ which give the corresponding vapour composition at a common total pressure.

recorded at 30-second intervals then, later, every 5 minutes for one hour, in most cases. The outputs of the vaporizer with the 3 : 2 and 1 : 1 mixture were only measured at the 70° setting. In one case, the vaporizer setting was altered several times during the experiment (Fig. 3). Laboratory temperature varied between 22° and 24°C. There were at least two series to confirm the reproducibility of the results for each setting.

Sampling was from two points along the tubing, 50 cm apart, which gave the same readings. Moving the probe tip within the tubing did not alter readings; thus, it is likely that the saturated vapour and diluent air coming from the vaporizer were properly mixed before sampling. The method of purging the tubing did not affect

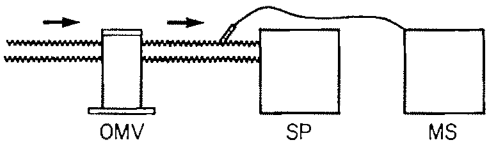


Fig. 2. Box diagram of the apparatus determining the output from the Oxford Miniature Vaporizer (OMV). MS, mass spectrometer; SP, Starling respiration pump.

the absorption or release of vapour from the tubing.

Results

These are shown in Figs 3 and 4. In Fig. 4(g) the temperature of the outside of the OMV was 22°C at the beginning and 13.5°C after one hour, giving some idea of the amount of cooling that took place. In Fig. 4(f) there was 8 ml of liquid left in the vaporizer bowl after 80 minutes; in Fig. 4(c) there was 15 ml left after 90 minutes.

Drawover anaesthesia with a 3:1 halothane/trichloroethylene mixture

The basic feasibility of the technique was assessed in four unselected patients from a general surgical list who were anaesthetised with a 3:1 halothane/trichloroethylene mixture. The only provisos were that the patient should breathe spontaneously and should not be grossly unfit and that the operation should not be expected to last more than one hour. The equipment consisted of the OMV attached to an Oxford Inflating Bellows with an Ambu anaesthetic non-rebreathing valve next to a facemask or tracheal tube (the components were joined with polythene tubing). Oxygen was added at 1 litre/minute into a metre length of tubing on the inlet side of the OMV, giving an $F\text{I}O_2$ of between 0.4 and 0.6, depending on the pattern of breathing. Expired minute volume was measured with a Wright electronic respirometer and the inspired halothane and trichloroethylene concentrations measured with the mass spectrometer. However, only in one patient was it possible to obtain a permanent trace of the inspired vapour concentrations. (Fig. 5.)

Modified anaesthetic records for two of the patients are shown in Figs 5 and 6. One of the four patients had a turbulent anaesthetic. He was a 63-year-old 86kg smoker having surgery for varicose veins. Premedication consisted of papaveretum 15 mg and hyoscine 0.3 mg. After thiopentone and suxamethonium for induction and intubation he failed to settle; he strained and coughed and thus did not breathe enough. He was therefore given more muscle relaxant and his lungs were ventilated with the vaporizer setting reduced to 30°; the anaesthetic then continued uneventfully to the end of the procedure 45 minutes later. In all other respects, the anaesthetics seemed good. The tachypnoea sometimes seen with trichloroethylene alone was not seen in these patients. Emergence in all cases was uncomplicated; there was no shivering, vomiting, nausea or complaint of pain. The speed of recovery seemed as quick as with usual anaesthetic techniques, and the recovery staff made no adverse comments. The patients were visited 4 hours later and none reported any adverse effects from anaesthesia.

Discussion

Raoult's Law[5] (see Appendix) describes how, at constant temperature, the vapour pressure of a solvent is lowered by the presence of a solute. If the components of the system behave as an ideal mixture (and few in practice do), then the total vapour pressure of the liquid will be linearly related to the mole fraction of solvent present.

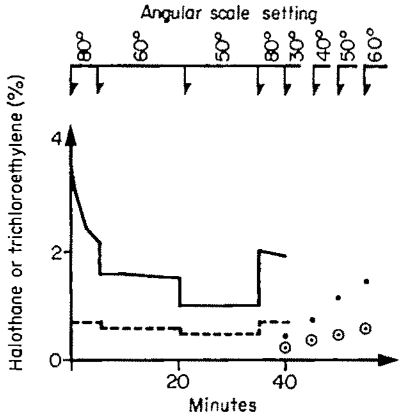


Fig. 3. Concentrations of halothane (——) and trichloroethylene (——) produced simultaneously from an OMV. Angular scale settings on the vaporizer and the initial starting proportion of halothane to trichloroethylene are shown. For further detail, see text.

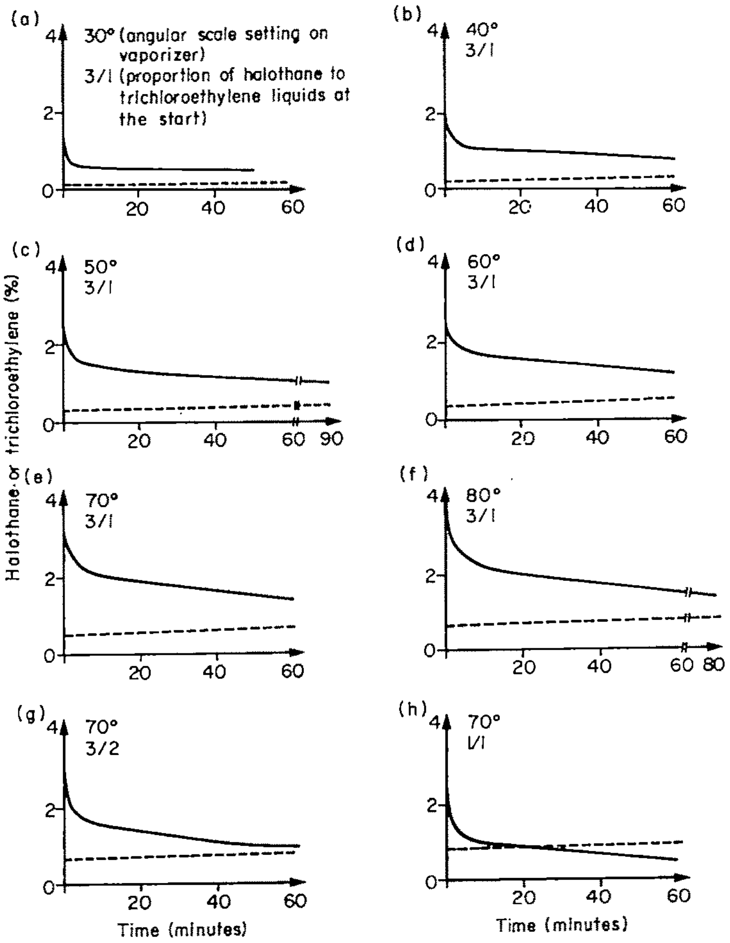


Fig. 4. The effect of altering the angular scale setting on halothane (H) and trichloroethylene (TCE) concentration during a single administration. Starting proportion H to TCE is 3:1. (——·), Halothane; (--⊙), trichloroethylene.

This is shown by line L in Fig. 1, calculated for the halothane and trichloroethylene pair assuming that they obey Raoult's Law. A corollary of this law is that for any given liquid mixture, the vapour above it will be richer in the more volatile liquid—in this case halothane. Curve V in Fig. 1 shows the proportion of each agent in the vapour phase above any liquid proportion, again calculated assuming that they behave as an ideal liquid pair.

An azeotrope is a liquid mixture of constant boiling point at a given pressure; thus, the liquid and the vapour phases have the same molar proportions of the two components of the mixture unless the ambient pressure is changed. For example, water and ethanol have an azeotropic mixture of 95% ethanol and 5% water at normal atmospheric pressure. This would be shown on a vapour composition diagram by coincidence of the liquid and vapour curves.

The results of the experiments show that there is no tendency to form an azeotrope, at least between 5% and 95% halothane in trichloroethylene (the extremes were not studied). In fact, the mixture behaves quite closely to an ideal liquid; compare ● with line L and ○ with curve V (Fig. 1). There is no evidence that the two agents react chemically with each other (information from ICI).

Halothane and trichloroethylene do not

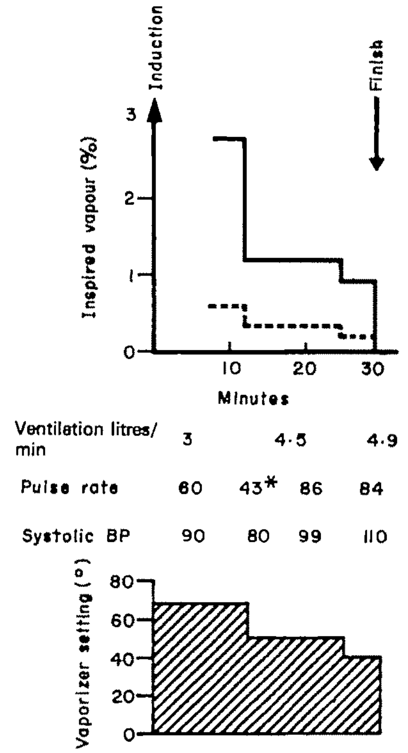


Fig. 5. Modified anaesthetic record for a patient breathing spontaneously a 3:1 H and TCE mixture. Patient A. A 23-year-old female, ASA 1, 58 kg. Removal of breast lump. Premedication: papaveretum 15 mg and hyoscine 0.3 mg. Induction: thiopentone 350 mg. Maintenance: halothane and trichloroethylene mixture, starting with a 3:1 ratio in oxygen-rich air.

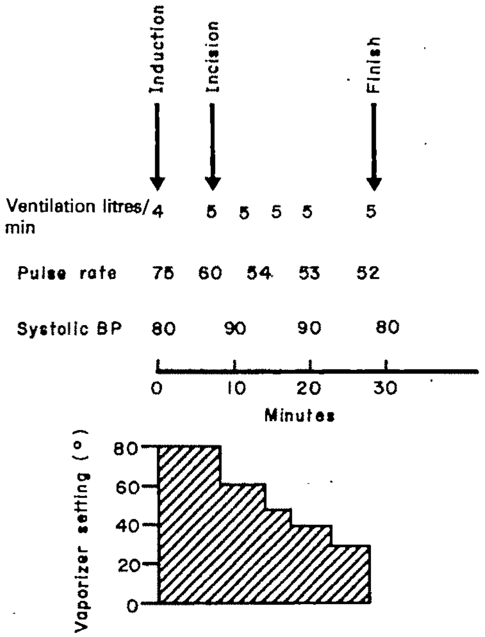


Fig. 6. Modified anaesthetic record for a patient breathing spontaneously an H and TCE mixture. Inspired vapour concentration measured with a mass spectrometer. Patient B. A 65-year-old female, ASA I, 66 kg. Removal of large lipoma on chest wall. Premedication: papaveretum 10 mg and hyoscine 0.2 mg. Induction: thiopentone 200 mg. Maintenance: halothane and trichloroethylene mixture, starting with a 3:1 ratio in oxygen-rich air. *, Atropine 0.6 mg given intravenously for a pulse rate of 43 beats/minute. (——), Halothane; (——), trichloroethylene.

form an azeotrope so their proportions change continuously as they are vaporized. This is seen in Fig. 4, where for a given starting composition the halothane concentration decreases over a period while the trichloroethylene concentration increases. In addition, a fall in temperature of the OMV (which is only thermostabilised) lowers the output of halothane more than that of trichloroethylene. When giving an anaesthetic, this effect of cooling is reduced because the minute volume of the patient is often less than the 5.2 litres/minute of the Starling pump. Furthermore, if low settings are used on the vaporizer, the tendency to cool will also be reduced. The 3:1 starting ratio was chosen for the patient studies because it was considered that this would be the most useful; an adequate quantity of halothane is needed at the beginning of the administration, to establish a reasonable depth of anaesthesia rapidly. That the halothane output becomes less with time, fortunately matches the general requirements of inhalational anaesthesia. The more slowly increasing output of trichloroethylene does, in part, make up for this loss of anaesthetic potency.

When using the Triservice equipment, where the trichloroethylene is given through a separate vaporizer from the halothane, it has been recommended that the trichloroethylene can be left at 1% as a 'nitrous oxide substitute' and the depth of anaesthesia adjusted by altering the halothane output. Clearly, that degree of flexibility is not possible when the source of both agents is from a single vaporizer as one has no control over their relative proportions, except by selecting the initial starting ratio. In practice, this does not seem to matter and one adjusts the depth of anaesthesia in the normal way, according to the signs of the patient.

Conclusions

The use of two suitable vaporizers is probably the best way of administering mixtures of halothane and trichloroethylene, although the predictability of the vapour output may not be as good as one might first think. If the vaporizers are in series, vapour from the upstream one will always dissolve in the liquid in the downstream one. However, if necessity, expense or weight made it expedient to have only one vaporizer, the method of mixing described produces good anaesthetic for drawover anaesthesia, which is superior to halothane alone. It would also be applicable to other simple vaporizers, e.g. the Goldman or improvised ones.[6] The use of Fig. 4 may assist those wishing to estimate approximate concentrations of vapour produced.

Acknowledgments

I wish to thank Mr R. Tennant, Senior Technician of the Magill Department of Anaesthesia, for his considerable practical help and Professor C.M. Conway and Dr T.B. Boulton for their helpful criticism. Part of the funding for this work was by a grant from the Special Trustees of the Westminster Hospital.

References

1. Hall RM, Boulton TB. Editorial. *Anaesthesia* 1979; **34:** 755–6.
2. Gabbe D, Ozorio HPL. Halothane–trichloroethylene and air. *Anaesthesia* 1968; **23:** 705–6.
3. Knight RJ, Houghton IT. Field experience with the Triservice anaesthetic apparatus in Oman and Northern Ireland. *Anaesthesia* 1981; **36:** 1122–7.
4. Houghton IT. The Triservice anaesthetic apparatus. *Anaesthesia* 1981; **36:** 1094–108.
5. Gucker FT, Seifert RL. In: *Physical chemistry* London: English University Press Ltd, 1967, 460.
6. Boulton TB. Anaesthesia and resuscitation in difficult environments. In: Hewer CL, ed. *Recent advances in anaesthesia and analgesia*, 11th edn. Edinburgh and London: Churchill Livingstone, 1972: 143.

Appendix

A note on Raoult's Law

Raoult's Law states that at constant temperature the vapour pressure p_1 of a solvent equals that of the pure solvent, $p_1{}^\circ$, multiplied by its mole fraction, x_1

$$p_1 = p_1{}^\circ x_1 \text{ (T const).}$$

Applied to a mixture of two substances, the total vapour pressure of the mixture, p, is a linear function of either component in the liquid phase, i.e.:

$$p = p_1{}^\circ x_1 + p_2{}^\circ x_2.$$

where subscripts 1 and 2 refer to the two agents. The mole fraction of agent 1 in the vapour phase, x_1', is given by

$$x_1' = \frac{p_1}{p} = \frac{p_1{}^\circ x_1}{p_1{}^\circ x_1 + p_2{}^\circ x_2}.$$

At 20°C $p^\circ = 32.3$ kPa for halothane and 7.88 kPa for trichloroethylene. Line L and curve V in Fig. 1 were derived from these equations.

Anaesthesia, 1986, Volume 41, pages 316–320

APPARATUS

Clinical automatic control of neuromuscular blockade

A. J. ASBURY AND D. A. LINKENS

Summary

A simple feedback control technique has been used to automatically deliver pancuronium to anaesthetised surgical patients. The dosage rate is automatically adjusted at 10-second intervals, according to the measured evoked, rectified, integrated electromyogram. When set to demand 80 percent blockade, in 40 patients, the controller maintained blockade at a steady mean level of 72.9 percent (consuming pancuronium at a mean rate of 0.47 μg/kg/minute). The main clinical practical problems involved protection against electrical noise and the need to spend time setting up the equipment.

Key words

Anaesthetic techniques; automated.
Neuromuscular relaxants; measurement of response.

One of the problems of using neuromuscular blocking drugs is that there is a considerable variation in individual response and, in the absence of effective monitoring, overdosage may occur. One strategy to avoid overdosage is to give a modest loading dose and then several small increments, according to the response. This can, however, considerably increase the workload of the single-handed anaesthetist. An alternative solution is to use closed-loop feedback control of drug dosage, whereby the measured degree of neuromuscular blockade is used to automatically control the inflow of the neuromuscular blocker. This method ensures that the dose of relaxant is continuously adjusted according to the patient's response.

Unfortunately, control systems can also have problems; for example, they may become unstable when absolute time delays are introduced, or when changes in total system gain occur. Furthermore, even the most simple proportional controller requires the user to make some assumptions about the patient's drug handling and these have to be incorporated into the controller design as gains and time constants. Even if the correct values for that patient have been assumed, surgery may, by producing new tissue spaces and bleeding etc., cause changes in the initial values with which the controller may be unable to cope causing it to become unstable. The final problem is that blockade monitoring, using electromyography (EMG) is liable to interference from diathermy and the mains electricity supply. This may be merely irritating when only monitoring is involved, but in a closed-loop system there is a risk that the patient may be given doses

---

A.J. Asbury, MBChB, PhD, FFARCS, Senior Lecturer in Anaesthesia and Hon. Consultant Anaesthetist, University Department of Anaesthesia, Western Infirmary, Glasgow G11 6NT, Professor D.A. Linkens, BSc (Eng), MSc, PhD, FInstMC, MIEE, AGCI, CEng, Department of Control Engineering, University of Sheffield, Sheffield.
Correspondence should be addressed to: Dr A. John Asbury, please.

0003–2409/86/030316 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

according to incorrect information.

The object of the present study was to evaluate whether a simple proportional feedback controller could manage the control of neuromuscular blockade under clinical conditions.

Methods

The nature and risks of the study were explained to the patients and they signed consent forms approved by the local Hospital Ethical Committee. Forty patients, ASA I or II, who presented for major elective surgery were studied. Patients with abnormal sensitivity to anaesthetic drugs or with any neurological or muscle disorder were excluded from the study. Patients receiving drugs known to affect neuromuscular transmission were also excluded.

The electrical circuitry of the controller has already been described in detail elsewhere.[1] In essence, a supramaximal electrical stimulus is delivered to the ulnar nerve at the elbow at 10-second intervals and this evokes a contraction of the small muscles of the hand and produces an EMG (Fig. 1). The EMG is rectified, integrated and then presented to the controller as a steady DC voltage (RIEMG). The RIEMG is then compared with the voltage representing the desired RIEMG (effectively the inverse of the level of paralysis), and the difference which is termed 'the error' signal is used to power a simple peristaltic pump. The pump delivers the diluted neuromuscular blocker (in this case pancuronium 50 μg/ml) via a sterile fluid path to the patient. The feedback system therefore resets the drug dosage regularly at 10-second intervals, according to the RIEMG. Circuitry was included so that if diathermy interference was detected, the previous RIEMG would be held until the next stimulus–RIEMG cycle.

This simple controller is of proportional design where the infusion rate is directly controlled by the error signal, and like all proportional controllers, will not produce the exact steady level of blockade demanded. This is a predictable result from mathematical analysis and the nature of this particular type of controller.

The anaesthetic technique and method of feedback control

Patients were premedicated with Mist Mag Trisil, 30 ml orally, one hour pre-operatively. In the anaesthetic room a cannula was inserted in the right cephalic vein and connected to an infusion of saline running at 4 ml/kg/hour, and adjusted according to the fluid loss during the operation. The left cephalic vein was cannulated for connexion to the pump which delivers the pancuronium.

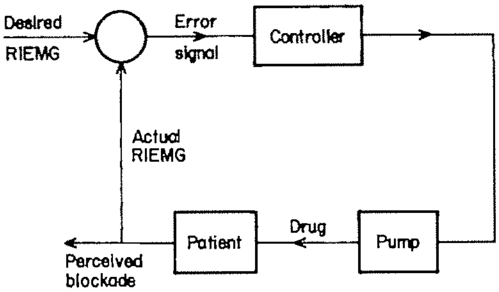


Fig. 1. A block diagram of the feedback controller and patient system.

The stimulating and recording electrodes were sited on the left arm, after the skin had been prepared by the following method. The skin was first degreased with alcohol and then gently abraded with glass paper and then finally cleaned again with alcohol hibitane mixture. The electrodes, which were made of lead sheet 1 cm × 3 cm, were then coated with conductive jelly and appliedwith adhesive tape and allowed to settle.

Droperidol, 0.14 mg/kg was then administered, followed by fentanyl 3.5 μg/kg. The anaesthetic induction was then completed with an intravenous injection of methohexitone 0.9 mg/kg and suxamethonium 0.5 mg/kg. After tracheal intubation the patients' lungs were inflated with a 66% nitrous oxide in oxygen mixture. When the position of the tracheal tube had been checked, the patient was taken into the operating theatre. In all cases, the patient could be easily ventilated, the fentanyl having rendered the patient apnoeic. The patient was connected to a Cape ventilator and the tidal volume adjusted to give an end exhaled carbon dioxide concentration of between 3.8 and 4.2%, measured with a Datex Normocap. Further doses of droperidol and fentanyl were administered during the operation as clinically indicated.

The stimulating and recording electrodes were then connected and the evoked electromyogram inspected on an oscilloscope. This is an essential step; if only the EMG results were checked after integration and rectification, then any spurious signal (e.g. from the mains) which might be included in the integration, could be overlooked.

When the RIEMG was steady (i.e. 0% paralysis), the controller was set to the desired level of blockade (80% in this instance) and the loop closed. The patient was then given an intravenous injection of pancuronium 20 μg/kg. The RIEMG and the voltage applied to the pump, which was directly proportional to the rate of inflow of pancuronium, were continuously recorded on a chart recorder. The volume consumed, as measured from the burette, was also recorded manually at 5-minute intervals. At the end of the operation, the residual neuromuscular blockade was reversed with the controller off, and when the patient was breathing he was transferred to the recovery room for routine monitoring. Specific enquiries were made in the postoperative period, to determine whether the patient had any problems related to the electrode siting or stimulation.

Calculations and statistics

The time taken to achieve a steady state was measured as the time from the loading injection of pancuronium to when the level of blockade, after exceeding the desired level, again dropped below the desired level (Fig. 2). The steady state was deemed to have commenced at this point and to have terminated when the loop was opened.

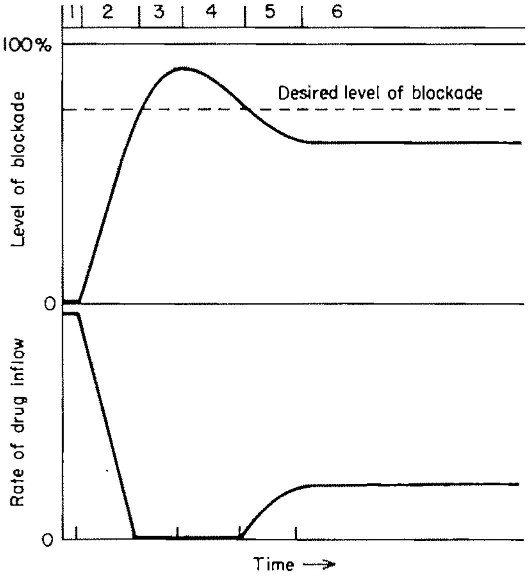


Fig. 2. A graph showing the general form of response to requests to bring blockade to 80%.

The features of steady state blockade were quantified by calculating the mean, standard deviation and coefficient of variation of the 5-minute blockade points. The steady state consumption was calculated from the 5-minute burette readings, which were checked against the voltage trace. The relationship between the steady state neuromuscular blockade and the consequent consumption was examined using linear regression.

Results

Forty patients were studied, 20 male and 20 female and their ages ranged from 16–77 years with a mean of 55.3 years (SD 16.7). The patients' weights ranged from 22–103 kg with a mean of 63.7 kg (SD 12.3). All the cases involved major abdominal surgery including cholecystectomy, vagotomy, and various bowel resections. All the patients were biochemically and haematologically normal. The blood loss in all cases was never enough to necessitate blood transfusion. No patients described any discomfort attributable to the electrodes or the stimulation in the postoperative period.

Figure 2 is a diagram showing the form of response followed by all the patients except numbers 30, 33 and 35. Patient 30 never exceeded the desired level of blockade and went effectively from phase one to phase six. In this patient, the point at which the steady state was deemed to have occurred was estimated by eye. In patient 33, there was a slow sinusoidal oscillation in phase six of about 20 minutes period, centering on the mean blockade level of 73.3%. In the study on patient 35, the pump winding broke and when the sterile fluid path had been restored the patient's blockade had nearly levelled out; after a further 5 minutes, it had settled down at 74.3% and it continued at this level for a further 80 minutes.

Figure 3 is a histogram showing the dose administered until the controller had produced a steady level of blockade. There is no obvious reason for the bimodal distribution; the mean is 47.1 μg/kg. In spite of this, the time to steady state showed a unimodal distribution ranging from 3–18 minutes with a modal value of 7 minutes and a mean of 8.39 minutes.

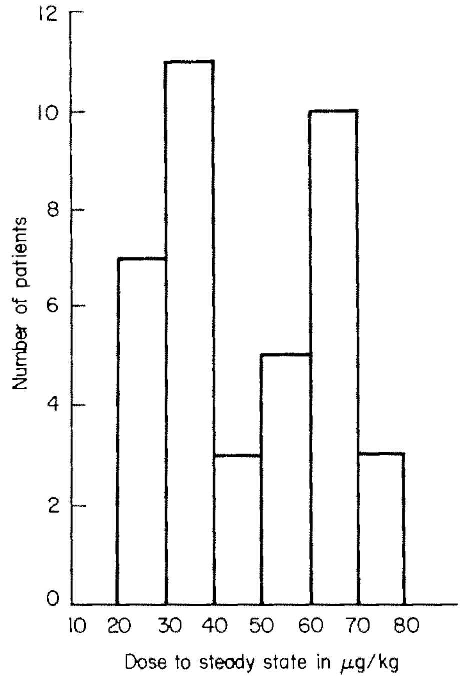


Fig. 3. Frequency histogram showing the dose of pancuronium before steady state occurred, including the 20 μg/kg loading dose. One case, the one in which the pump winding broke, is not included in this histogram.

Steady control was achieved for periods ranging from 30–230 minutes and, during this time, the mean blockade level was 72.92% (SD 3.13), with a range from 62.1–79.0%. The mean pancuronium consumption in steady state was 0.47 μg/kg minute (SD 0.23 μg/kg/minute) with results ranging from 0.07–1.6 μg/kg/minute. The coefficients of variation of blockade measured at 5-minute intervals, a measure of the steadiness of blockade, ranged from 0.6%–6.9% with two outlying results at 9.1 and 11.4%. These two results are deceptive, being caused by long period, low amplitude, damped sinusoidal oscillation about a steady mean value.

Examination of the relationship between steady blockade level and steady consumption using linear regression, produced a correlation coefficient of 0.085, which was not significantly different from zero. No studies were abandoned due to self-sustaining oscillation, and in all patients residual neuromuscular blockade reversed easily with neostigmine.

Discussion

When neuromuscular blockade control is initiated, a response similar to that shown in Fig. 2 is seen. Phase one is variable in length and depends on the extent to which it is necessary to saturate the margin of safety for neuromuscular transmission above the level produced by the loading dose of 20 μg/kg. If the feedback controller sees that no blockade has resulted from the loading dose, then the rate of pancuronium inflow will rise rapidly to a maximum, where it will stay until blockade begins to occur in phase two. The rate of pancuronium inflow then decreases and reaches zero when the level of blockade crosses the desired level. Phase three is a result of the interval between the injection of the neuromuscular blocker and the perceived response. The rate of injection runs ahead of the requirements in phase two and causes an overshoot in phase three. In phase four, the excess pancuronium is metabolised and, as soon as the level of blockade returns to the desired level, the inflow of pancuronium recommences in phase five, and eventually reaches a steady level in phase six. In this phase, the steady level of blockade indicates an equilibrium situation, whereby the amount of pancuronium injected balances that removed by metabolic and distributive processes.

The low coefficients of variation of blockade suggest that it is possible to maintain blockade at a steady level with a fairly high degree of precision. In practical terms, this is more than is surgically necessary. Unfortunately, one cannot predict, with such a simple proportional controller, exactly what the level will be. This problem could be easily rectified by the addition of an integral circuit, but at the risk of assuming more information about the patient.

The major practical problems of using this technique in the operating theatre relate to the theatre environment, and the need to ensure that operating lists run efficiently. In the cases described, there were no problems with diathermy or mains interference. However, some delay was experienced because of the time it took to set up the equipment and the need to make control readings in the unparalysed state. This requirement could be removed in future modifications of the equipment, by the use of the 'train-of-four technique' to detect neuromuscular blockade.

We were particularly interested at the outset in looking at the practicalities of feedback control of neuromuscular blockade in the operating theatre and, since these studies, new intermediate duration non-depolarising relaxants such as atracurium and vecuronium have become available. If this type of technique was to be used more generally, these agents would be more suitable.

Conclusions

Feedback control of neuromuscular blockade is clinically feasible and can maintain a level of blockade automatically with precision far beyond that which is clinically required. Drugs such as atracurium or vecuronium would probably be a better choice than pancuronium in this situation. Setting up time is a minor problem, but this could be minimised by using train-of-four monitoring (each train acting as its own control) and commercial EMG monitors, such as the Datex Relaxograph.

Acknowledgments

The authors gratefully acknowledge the assistance and encouragement of Mr J.A.R. Smith (Consultant Surgeon) who allowed them to study his patients and Mrs J. Buttar who typed the manuscript.

Reference

1. Brown BH, Asbury AJ, Linkens DA, Perks R, Anthony M. Closed-loop control of muscle relaxation during surgery. *Clinical Physics and Physiological Measurement* 1980; **1:** 203–10.

Anaesthesia, 1986, Volume 41, pages 321–338

Correspondence

Accuracy of the Datex Normac anaesthetic vapour analyser 322
A. Synnott, FFARCSI and W.S. Wren, FFARCS
Recurrent failure of a monitored dial mixer 323
P. Dodge, BSc and A. Sinclair, PhD.
A.S. Murphy 323
Emergency anaesthesia in a patient with plasma cholinesterase deficiency 323
P.J. Morrison, BM, BS, BMedSci, P.N. Robinson, FFARCS, and K.G.A. Macleod, FFARCS
Eclampsia and haemorrhage in a Jehovah's Witness 324
M.F. Reid, FFARCS, K. Nohr, MB, ChB, and R.J.S. Birks, FFARCS
Depression and anxiety in pain clinics 325
I.M.C. Clarke, FFARCS, and Daphne Barnes, MSc,MRCPsych.
G.W. Hanks, MRCP and J.W. Lloyd, FFARCS 326
The 'wake-up' test 327
N. McC. Schofield, FFARCS,
P.A. Tomlinson, FFARCS, P.M. Yeoman, FFARCS, A.D. Jardine, FFARCS and J.K. Webb, MB, BS, FRCS 327
Elizabeth G. Bradshaw, MD, FFARCS 328
Biochemical changes associated with suxamethonium 328
H.F. Drake, FFARCS and W.A. Yanny, FFARCSI
A.S. Laurence, FFARCS 328
Formalin toxicity in hydatid liver disease 329
J. Papadimitriou, MD and L. Papadimitriou, MD
A.R. Aggarwal, MD, DA and R.L. Garg, MD 329
High frequency jet ventilation through a Robertshaw double lumen tube 330
C.J. Mason, FFARCS
Hallucinations after oral lorazepam in children 330
A.A. Van den Berg, FFARCS
Puncture of the ascending aorta—a complication of subclavian venous cannulation 331
D. Childs, FFARCS and R.G. Wilkes, FFARCS
Difficult tracheal intubation 332
I.D. Levack, MD, FFARCS and A.H.B. Masson, FFARCS
Difficult tracheal intubation in obstetrics 332
R.S. Cormack, FFARCS
Urban hypothermia 333
E.L. Lloyd, FRCPE, FFARCS
N.V. Ferguson, FFARCS 333
Epidural test dose 334
S. Mallaiah, FFARCS
Eye to eye with Murphy's law 334
R.G. MacGillivray, FFA(SA) and J.A. Odell, FRCSE
The end of the crystalloid era? 335
P.J. Horsey, FFARCS
P. Cox, FFARCS 335
K. Hillman, FFARCS, FFARACS 336
Transient loss of consciousness after therapeutic epidural injection 336
D.C. Moore, MD
Labels for drug ampoules 337
B.P. Guratsky, FFARCS
Nasotracheal intubation 337
M.J. Harrison, FFARCS
Equipment for paediatric epidurals 337
J. Desparmet, MD
Inhalation of a minitracheotomy tube 338
A.B. Leach, FFARCS

All correspondence should be addressed to Dr J.N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

Letters must be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters contained in 'Notice to Contributors' to *Anaesthesia* printed at the back of each issue. The degrees and diplomas of each author must be given in a covering letter personally signed by all the authors.

Accuracy of the Datex Normac anaesthetic vapour analyser

In their recent evaluation of the Datex Normac anaesthetic vapour analyser (*Anaesthesia* 1985; **40:** 555–9) Luff and White state that the frequency response of the instrument precludes the accurate measurement of end-tidal vapour concentrations at respiratory rates in excess of 15 breaths/minute.

We have recently reassessed the accuracy of this instrument over a range of respiratory frequencies, in a bench test. A solenoid (Siemens test-gas valve) was interposed between the anaesthetic system connector of the Datex analyser, and the Y-connector at the distal (patient) end of the patient system of a SV900C ventilator (Siemens). This device permits the delivery of an alternating flow of two gas mixtures to the analyser, by delivering different gas mixtures to the ventilator and the test valve at a range of respiratory frequencies which vary from 2–120 minute. The test was performed with the following pairs of gas mixtures, using previously calibrated mixtures of halothane or isoflurane in oxygen: 1 percent halothane and 0 percent halothane; 2 percent halothane and 1 percent halothane; and 2 percent halothane and 1.5 percent halothane, and the entire sequence was then repeated with isoflurane. The electrical output of the Normac was input to a microcomputer, which recorded the peak and trough values (equivalent to inspired and end-tidal values respectively).

The results for all mixtures were similar and are depicted in Fig. 1, which confirms the accuracy of the Normac at frequencies of up to 15 breaths/minute. At frequencies above this, the instrument tends to underestimate the inspired concentrations and overestimate end-tidal values, and the magnitude of the error is 5 percent at frequencies of 28 breaths/minute and 10 percent at frequencies of 38 breaths/minute. Thus, if the instrument displays an end-tidal halothane value of 1.0 percent at f 28, the true value is 0.95 percent and the true value for a displayed value of 1.0 percent at f 38 is 0.9 percent.

However, since these inaccuracies have proved to be quantitatively predictable it has been possible to incorporate the correction factors required to compensate for them into a simple computer program. The output of the Datex vapour analyser in use in this department is, therefore, displayed on a microcomputer screen (BBC), in accurate digital values (with end-tidal levels in the form of percentage and MAC values) for a range of respiratory frequencies up to 40 breaths/minute. The program assumes an I:E ratio of 1:1 which is commonly encountered in children with respiratory frequencies of 17–33 breaths/minute during anaesthesia,[1] and, in the unlikely event of an I:E ratio of 1:2 developing at these frequencies, a further correction factor is applied.

The findings of this test, therefore, agree with those of Luff and White, but it is nonetheless evident that the Datex Normac vapour analyser can be used with the accuracy required for clinical purposes at respiratory frequencies of up to 40 breaths/minute, if two simple correction factors are applied to the display values, and with the accuracy required for research purposes if the computerised system described above is employed.

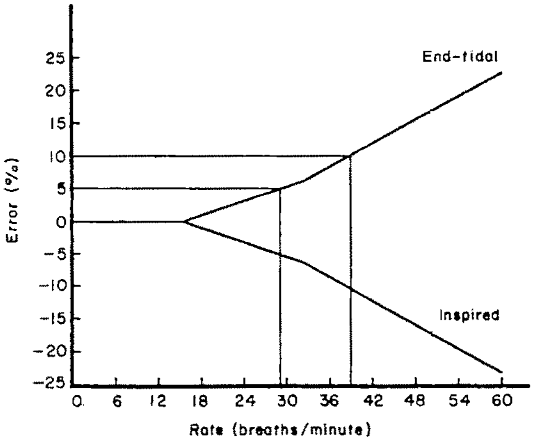


Fig. 1.

Most of the vaporizers in current use are inaccurate and unpredictable in their delivery, particularly when changes in the carrier gas composition occur during anaesthesia.[2–4] Clinical precision and economy in the use of expensive volatile agents therefore demands that their dosage is regulated by accurate end-tidal measurements; it is reassuring to know that this analyser need not be discarded.

Department of Anaesthetics, A. Synnott
Our Lady's Hospital for Sick Children, W.S. Wren
Crumlin,
Dublin 12

References

1. Byrick RJ, Janssen EG. Respiratory waveform and rebreathing in T-piece circuits. A comparison of enflurane and halothane waveforms. *Anaesthesiology* 1980; **53:** 371–8.
2. Palayiwa E, Sanderson MH, Hahn EW. Effects of carrier gas composition on the output of six anaesthetic vaporizers. *British Journal of Anaesthesia* 1983; **55:** 1025–37.
3. Wren WS, Allen P, Synnott A, O'Griofa P. Effect of nitrous oxide on the respiratory pattern of spontaneously breathing children during anaesthesia—A reappraisal. *British Journal of Anaesthesia* (in press).
4. Synnott A, Wren WS (Unpublished observations). The effects of nitrous oxide on the output of three halothane analysers. Submitted to the *British Journal of Anaesthesia* 1985.

Recurrent failure of a monitored dial mixer

We would like to bring to your readers' attention our experience with a proportional gas mixer (monitored dial mixer) manufactured by Frazer Harlake in the United States and Cyprane in England. These mixers have been incorporated into a number of anaesthesia machines.

In early 1979, the Health Protection Branch received a problem report from a Canadian hospital, describing the failure of a monitored dial mixer (MDM) manufactured by Frazer Harlake. The brass drive stem nut in the flow control knob assembly had stripped, causing a complete cessation of the flow of anaesthetic gases to a patient during an operation.

The manufacturer agreed, after discussions with the Bureau of Medical Devices, to resolve the problem, and the following design changes in the flow control knob assembly were made. The brass nut was replaced with an aluminium bronze nut, a retaining ring with washer was included to limit the motion of the control knob from approximately 11 turns to six and a half turns and a change in the type of lubricant was made.

These modifications were made to all new units distributed in Canada by Ohmeda (formerly Medishield) after January 1981. A letter was sent at that time by Ohmeda, urging all customers to have their units modified. Over 700 units have since been corrected. A similar failure of the brass drive stem nut on an MDM unit has been reported by Klein and Ali.[1]

In late 1983, the Branch received a report that an identical failure of the MDM gas mixer had occurred during an operation. Further investigation revealed that four out of five units at the hospital showed signs of similar mechanical failure. These MDM units were manufactured by Cyprane, England, who were still supplying unmodified flow control assemblies containing the brass nut. The affected Cyprane units were imported from Medical and Industrial Equipment, England (MIE) and distributed by MIE Canada. The distributor was unaware of the regulatory action underway with this product, presumably because of the indirect supply path. However, they took prompt action when advised of the hazards. The entire mixer was replaced in all anaesthesia machines sold in Canada by MIE. Cyprane now supplies all new flow control assemblies with the above modifications.

Since Cyprane failed to provide details on the time frame and extent of their modifications, we are uncertain as to the remedial steps taken in other countries. What we do know is that Cyprane's modifications lagged those undertaken by Frazer Harlake and that their customer base was not informed. We therefore recommend that your readers confirm with their suppliers whether existing mixers are within current specifications.

Bureau of Medical Devices,
Environmental Health Centre,
Tunney's Pasture,
Ottawa, Ontario Canada K1A 0L2

P. Dodge
A. Sinclair

Reference

1. Klein SL, Ali NMK. An unusual occurrence of total anaesthesia machine failure during administration of an anaesthetic. *Anesthesiology* 1982; **57**: 328–30.

A reply

Thank you for the opportunity of commenting on this letter.

We became aware of this problem as a result of a report[1] and the service organisation was instructed on its diagnosis and rectification. We subsequently modified the design of our MDM mixers in late 1983 and incorporated a number of improvements to the flow control system, including the introduction of an aluminium bronze nut. Service kits to enable the upgrading of the flow control system were shipped to our Service Centres, with instructions to upgrade products at the next machine service. Additionally, all new production from January 1984 incorporated the improved flow control mechanism.

We are therefore confident that all regularly serviced machines will incorporate the improved version. However, if any readers have any doubts about their own equipment, please let us know and we will confirm the position with the appropriate service centre.

Sales Manager,
Ohmeda,
Steeton,
West Yorkshire BD20 6RB

A.S. Murphy

Reference

1. Klein SL, Ali NMK. An unusual occurrence of total anesthesia machine failure during administration of an anesthetic. *Anesthesiology* 1982; **57**: 328–30.

Emergency anaesthesia in a patient with plasma cholinesterase deficiency

A 36-year-old, 79 kg, gravida 2 patient with a history of a previous elective Caesarean section for breech presentation had a trial of labour. Four hours into labour an epidural was inserted for analgesia; a history taken at the time revealed that she had had one previous uncomplicated dental anaesthetic and that she was otherwise well. Approximately one hour later, the patient had a brisk vaginal haemorrhage and there were signs of severe fetal distress. Possible placental abruption was suspected and general anaesthesia for emergency Caesarean section was requested by the obstetrician; there was insufficient time to extend the epidural blockade. On repeat questioning, the patient revealed that a screening programme had shown her to be plasma cholinesterase deficient. The suitability of the emergency obstetric general anaesthetic technique was then called into question.

After necessarily brief consideration, the following management was decided upon. The patient was immediately given 30 ml magnesium trisilicate orally and transferred, in the left lateral position, to the theatre where she was placed on the operating table with a 20° left lateral tilt. Pre-oxygenation was commenced. Her clinical condition was stable and the intravenous infusion was running well. After 3 minutes, anaesthesia was commenced by giving a bolus dose of atracurium 55 mg (0.7 mg/kg), followed after 20 seconds by thiopentone 250 mg. Cricoid pressure was applied and, after a further 30 seconds, tracheal intubation was achieved with a size 8.00-mm cuffed Portex tracheal tube. A good view of the larynx was obtained which showed full relaxation of the vocal cords; intubation conditions were judged to be excellent. Anaesthesia was maintained using 50 percent nitrous oxide in oxygen with 0.5 percent halothane until delivery, after which pethidine 50 mg was given and the gas flows altered to 60 percent nitrous oxide in oxygen.

The child was delivered in a satisfactory condition; 1 and 5 minute Apgar scores were 7 and 10. The operation lasted 50 minutes and no further atracurium was given. The patient reversed uneventfully with neostigmine 2.5 mg and atropine 1.2 mg and the postoperative period was normal. The patient had no adverse comments to make either immediately or on the postoperative visit.

The possibility of this situation arising is of the order of 1:20 000 if one accepts a figure of 1:2000 for the occurrence of plasma cholinesterase deficiency and 1:10 for a Caesarean section.[1] This problem would normally be managed by the use of regional techniques; however, in this emergency, speed was important and general anaesthesia deemed mandatory. What is the correct management in this situation? We consider suxamethonium to be contraindicated in this case since 4–24 hours of paralysis may result following its use and, in the event of failure to intubate, the usual drill would be impossible; a tracheostomy might be required to protect the airway.

Another technique is to induce and maintain anaesthesia using inhalational agents throughout and to conduct anaesthesia, and the operation, with the patient in a left lateral position. This would further compromise the fetus and leave the patient's airway unprotected. The use of a non-depolarising relaxant to facilitate intubation should be part of the anaesthetic technique in this situation. Atracurium is probably the most suitable agent available since it rapidly produces good conditions with a reliable duration of paralysis.[2]

A recent development in the use of non-depolarising relaxants for the rapid sequence induction of anaesthesia may have been useful in this case: this has been termed the 'priming principle'. Advocates suggest that prior administration of 15–20 percent of the total calculated dose of non-depolarising muscle relaxant followed by the remainder with induction after a 3–6 minute interval may achieve a more rapid onset of paralysis with good intubation conditions.[3,4]

We would welcome discussion and comments on the management of this case.

Department of Anaesthesia,
St. Mary's Hospital,
Praed Street,
London W2

P.J. Morrison
P.N. Robinson
K.G.A. Macleod

References

1. Whittaker M. Plasma cholinesterase variants and the anaesthetist. *Anaesthesia* 1980; **35:** 174–97.
2. Schiller DJ, Feldman SA. Comparison of intubating conditions with atracurium, vercuronium and pancuronium. *Anaesthesia* 1984; **39:** 1188–91.
3. Schwarz S, Ilias W, Lackner F, Mayrhofer O, Foldes FF. Rapid tracheal intubation with vecuronium; the priming principle. *Anesthesiology* 1985; **62:** 388–91.
4. Mehta MP, Choi WW, Gergis SD, Sokoll MD, Adolphson AJ. Facilitation of rapid endotracheal intubations with divided doses of nondepolarising blocking drugs. *Anesthesiology* 1985; **62:** 392–5.

Eclampsia and haemorrhage in a Jehovah's Witness

Reports of death from haemorrhage occurring in Jehovah's Witnesses refusing blood products has drawn attention to the difficulties in treating these patients.[1,2] We have recently managed a case of disseminated intravascular coagulation (DIC) and serious haemorrhage in a Jehovah's Witness following eclampsia.

A 20-year-old primigravida was admitted in spontaneous labour at 37 weeks' gestation. On admission, her arterial blood pressure was 140/90 mmHg and urinalysis with haemoacombistix revealed significant

Table 1. Profile of postoperative haematological tests

Time after operation (hours)	Hb (g/dl)	Platelets (10^9/l)	Prothrombin time/ control (seconds)	Kaolin cephalin coagulation time/ control (seconds)	Fibrinogen (g/l)	Fibrinogen degradation products (μg/ml)
2	12.5	93	17/12	36/36	2.3	256
4	7.6	30	20.5/13	46.5/38	1.2	high
12	6.1	34	18/13	46/38	1.0	64
29	4.9	43	12/12	33/37	4.8	48
192	6.0	397	—	—	—	—

protein. She had no evidence of oedema. Epidural analgesia was suggested but declined, so intramuscular diamorphine and prochlorperazine were administered.

Two hours later the patient appeared stable, with blood pressure maintained at 140/90 mmHg. However, a sustained fetal bradycardia of 50–80 beats/minute was noted on the cardiotocograph, and it was decided to perform an emergency Caesarean section. The patient had a convulsion with a short period of apnoea whilst in transit. She had recovered consciousness on arrival in the operating room and was immediately anaesthetised using a standard general technique. The baby had an Apgar of 0 at one minute but was successfully resuscitated. The remainder of the operation was uneventful.

Postoperatively, serious haemorrhage occurred from the wound and vagina. The coagulation screen demonstrated DIC, with elevated kaolin cephalin coagulation time, prothrombin time, and fibrin degradation products, and with low platelets and fibrinogen (Table 1). The patient and her husband were approached regarding the use of blood products and they were both adamant that none should be used in any circumstances. Resuscitation was therefore continued on the intensive care unit with polygeline (Haemaccel) and crystalloid infusions to maintain urine output and central venous pressure, and 60 percent O_2 was given via a Ventimask. In addition, she received 2 g of methylprednisolone and small doses of papaveretum.

By 29 hours postoperatively the patient's haemoglobin had fallen to 4.9 g/dl. However, the severe haemorrhage had subsided and there had been a spontaneous resolution of the coagulopathy. During the first 24 postoperative hours she had received 4000 ml polygeline and 4000 ml of crystalloid fluid.

Ten days later both mother and baby were discharged home completely well. Five weeks postoperatively the mother's haemoglobin had recovered to 12.2 g/dl. She was already contemplating a second pregnancy.

This case describes the successful management of serious haemorrhage and coagulopathy in a Jehovah's Witness, without the use of blood products. We appreciate that the patient may well have died as a result of withholding this treatment, but we believe that the request of a rational adult patient to avoid specific therapy on religious grounds must be respected.

Department of Anaesthetics,
Royal Hallamshire Hospital,
Sheffield S10 2RX

M.F. Reid
K. Nohr
R.J.S. Birks

References

1. Harris TJB, Parikh NR, Rao YK, Oliver RHP. Exsanguination in a Jehovah's Witness. *Anaesthesia* 1983; **38:** 989–92.
2. Cundy JM. Jehovah's Witnesses and haemorrhage (letter). *Anaesthesia* 1980; **35:** 1013–4.

Depression and anxiety in pain clinics

We were interested to read the paper by Dr G.W. Hanks *et al.* (*Anaesthesia* 1985; **40:** 676–9), since it confirms our earlier findings[1] that doctors who are untrained in the psychiatric aspects of chronic pain patients fail to recognise psychiatric morbidity. This should, of course, not be too surprising, since there have been many papers published in recent years[2-4] which indicate that this also happens in other specialties. Our own studies[5] indicate that the incidence of psychopathology, particularly depressive illness (dysthymic disorder), in chronic pain patients is at least as high as that in neurological patients and, in a population currently under study, exceeds 50 percent.

Their use of a screening test is particularly noteworthy since our feeling has also been that a simple self-report test is required to identify these patients. Otherwise, it is very unlikely they will be recognised. It is therefore disappointing that they have selected the Hamilton scale. This was originally designed to score a standardised interview by a trained psychiatrist, relies heavily on the presence of somatic symptoms and fails to identify those patients with non-depressive psychiatric illness (approximately one-third of the mentally ill group). It may be appropriate for a psychiatric sample of patients, but this is certainly not the case with either neurological or pain clinic patients. The Montgomery-Asberg[6] Rating Scale relies far less on somatic symptoms and for this reason we have used it in chronic pain population studies in England. Unfortunately, the Montgomery-Asberg Depression Rating Scale requires a trained interviewer; we now, therefore, employ the General Health Questionnaire (GHQ). We feel that this is more appropriate as a self-report questionnaire seeking affective disorders than the Hamilton, even when the Hamilton is 'modified' for self-report and presented by computer. The GHQ was designed as a self-report questionnaire and requires only a pencil for its completion and scoring. It has been well validated in a variety of patient populations. We are currently validating it with a pain clinic population and will report on this in the near future.

Pain Clinic,
Department of Psychiatry,
University of Calgary,
Foothills Hospital,
Calgary,
Alberta T2N 2T9,
Canada.

I.M.C. Clarke
Daphne Barnes

References

1. Benjamin S, Barnes D. Can anaesthetists detect depression in pain patients. *IV World Congress on Pain*, Seattle, U.S.A., 1984.
2. Bridges KW, Goldberg DP. Psychiatric illness in inpatients with neurological disorders: patients' views on discussion of emotional problems with neurologists. *British Medical Journal* 1984; **289:** 656–8.
3. Gomez J, Dally P. Psychologically mediated abdominal pain in surgical and medical outpatient clinics. *British Medical Journal* 1977; **1:** 1451–3.
4. Maguire GP, Julier DL, Hawton KE, Bancroft JHJ. Psychiatric morbidity and referral on two general medical wards. *British Medical Journal* 1974; **1:** 268–70.
5. Barnes D, Clarke IMC. Screening for psychiatric morbidity in pain patients. *University of Calgary Annual Psychiatric Research Meeting*, 1985.
6. Kearns NP, Cruikshank CA, McGuigan KJ, Riley SA, Shaw SP, Snaith RP. A comparison of depression rating scales. *British Journal of Psychiatry* 1982; **141:** 45–9.
7. Goldberg DP, Cooper B, Eastwood MR, Kedward AB, Shepherd M. A standardized psychiatric interview for use in community surveys. *British Journal of Preventive and Social Medicine* 1970; **24:** 18–23.

A reply

We are grateful to Dr Clarke and Dr Barnes for drawing our attention to their earlier findings, although the meeting abstract to which they refer contains no data. It is difficult therefore to comment on their conclusions and we look forward to the publication of their results in due course.

We agree that the Hamilton Depression Scale is not ideal for screening patients with physical complaints. However, we do not feel that the General Health Questionnaire (GHQ) is particularly suitable either. The GHQ is long and rather unwieldy; it does not identify the nature of the psychiatric disorder, but merely indicates abnormality. Since our original study we have been using the Hospital Anxiety and Depression Scale[1], which was specifically designed for use in hospital medical outpatient clinics, and we have also further modified the Hamilton for use in patients with cancer. We have recently presented this work[2] and it is now being prepared for publication. We are confident that these are valid *screening* instruments for use in chronic pain patients.

A pencil is, of course, cheaper and simpler to use than a computer. In a similar analogy, a hot air balloon is cheaper and simpler to use than a jumbo jet. Computer-administered rating scales have a number of advantages over paper-and-pencil questionnaires.[3–7] Briefly these may be summarised as: reliability, reproducibility and standardisation of the interview, automatic data storage and retrieval (which obviates the need for the collation, extraction, coding and entering of data separately, with the attendant possibility of errors), less likelihood of incomplete responses (whereas with paper and pencil questionnaires, particularly if they are long, patients quite often fail to answer all the questions) and the ability to program the computer to interact with the patient and thus generate a more personal atmosphere.

We believe that this is a useful technique which should be more widely employed.

Royal Marsden Hospital,
London SW3 6JJ
G.W. Hanks

Oxford Regional Pain Relief Unit,
Abingdon Hospital,
Abingdon OX14 1AG
J.W. Lloyd

References

1. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica* 1983; **67:** 361–70.
2. Finlay-Mills B, Hanks GW, Ancill R. Computer-administered rating scales for depression and anxiety in patients with advanced cancer (Abstract). *Symposium on Current Research in Terminal Care*, Glasgow, June 1985, p. 16.
3. Slack WV, Hicks GP, Reed CE, Van Cura LJ. A computer-based medical-history system. *New England Journal of Medicine* 1966; **274:** 194–8.
4. Lucas RW, Mullin PJ, Luna CBX, McInroy DC. Psychiatrists and a computer as interrogators of patients with alcohol-related illnesses: a comparison. *British Journal of Psychiatry* 1977; **131:** 160–7.
5. Carr AC, Ancill RJ, Ghosh A, Margo A. Direct assessment of depression by microcomputer. A feasibility study. *Acta Psychiatrica Scandinavica* 1981; **64:** 415–22.
6. Carr AC, Ghosh A. Response of phobic patients to direct computer assessment. *British Journal of Psychiatry* 1983; **142:** 60–5.
7. Rogers D, Ancill RJ. Comparison of conventional and computerised Hamilton rating scale. Abstract. *British Association of Psychopharmacology, Xth Annual Meeting*, Jersey, 1984.

The 'wake-up test'

It was interesting to read the article by Chamberlain and Bradshaw, who described their infusion technique for achieving 'wake-up' during surgery for Harrington rod fixation of a traumatic lumbar fracture in a young adult (*Anaesthesia* 1985; **40:** 780–2). It is true that anaesthetic techniques for such cases are not easily found in the literature. All the descriptions of techniques for wake-up have been related to scoliosis surgery which is most commonly, though not exclusively, performed on children and adolescents, and is generally more extensive.

These details may account for some of the shortcomings of the techniques previously described when applied to adult victims of trauma. Heavy premedication in these young patients is employed for the patients' benefit and is a useful, but not an essential, part of the anaesthetic technique. Any of the anaesthetic sequences described can be used without premedication. Such premedication does, I think, facilitate induction of a degree of hypotension when it is generally regarded as advantageous to scoliosis surgery.

It is prudent for the anaesthetist to anticipate wake-up by about 30 minutes in neuroleptic techniques, to ensure that narcotic depression is reduced and neuromuscular blockade is incomplete, particularly if a peripheral nerve stimulator is not in use. In the case reported, reductions in the infusion rates were made 20 minutes before wake-up. In my experience, no problems have been observed with neuromuscular blockade using curare, however short the notice of wake-up, though narcotic depression has occasionally had to be partly antagonised. It is true that some patients have been more active on awakening than is desirable. Postoperative respiratory depression has never been a significant problem. The only case in which intermittent positive pressure ventilation of the lungs was required, was one of scoliosis secondary to a neuromuscular disorder and ventilation was commenced 24 hours postoperatively for progressive ventilatory insufficiency.

The description of a narcotic and relaxant infusion technique for Harrington instrumentation will be useful to those anaesthetists who are in the habit of using infusions for anaesthesia and have suitable hardware to hand. I would suggest, however, that anaesthetists who are occasionally called upon to anaesthetise patients, who require to be awoken, use a technique as closely related to their everyday practice as they can.

John Radcliffe Hospital,
Oxford OX39 DU
N. McC. Schofield

Reference

1. Schofield N. McC. Anaesthesia for spinal disorders. In: Loach A.B. ed., *Anaesthesia for Orthopaedic Patients.* London: Edward Arnold, 1983.

We were interested to read the case report by Dr Chamberlain and Dr Bradshaw concerning the 'wake-up test' and satisfactory use of drug infusions in a patient receiving spinal fusion (*Anaesthesia* 1985; **40:** 780–2).

We have employed the test in 40 patients undergoing anterior procedures for scoliosis (30) and kyphosis (10), aged 18 months to 45 years. The pre-operative visit was most important. It provided an opportunity to explain the 'wake-up test' to the patient and conduct a mock test at the bedside. This often yielded valuable information about the capacity of retarded patients to respond accurately and the presence of pre-existing neurological impairment (paresis) could be noted. Anaesthesia consisted usually of opiate medication, induction with Althesin (thiopentone is now used) maintenance with nitrous oxide/oxygen halothane 0.5 percent and fentanyl 3 μg/kg bolus following induction. Alcuronium 0.3 mg/kg was given to facilitate intubation and provide neuromuscular blockade for the early part of the operation; further doses were not administered.

Halothane was discontinued 20 minutes before the planned test. Manual ventilation with 100 percent oxygen was instituted and continued throughout the test period with 5 percent carbon dioxide given if necessary to achieve normocapnia. Cooperative patients were first asked to move both hands and, when this was observed, to move their feet. After completion of the test, anaesthesia was re-instituted with a further bolus of induction agent and IPPV continued with halothane 0.5 percent. In all cases, a satisfactory 'wake-up test' could be performed within 5 minutes. Five patients were unable to respond to verbal command because of youth (1) or mental retardation (4). In these cases, after confirming satisfactory neuromuscular function with a peripheral nerve stimulator, leg movements were produced by stimulation of their forearms.

Impaired spinal cord function was suspected if movements were severely reduced in one or both legs but normal in both hands, compared with the preoperative state. Three patients proved to have impaired spinal cord function on these grounds; two returned to normal with release of spinal distraction, the third required 3 weeks for recovery. Only one patient claimed recall. Unlike a number of cases, this patient had only required a single test which lasted just 2 minutes. She had felt neither discomfort nor anxiety, however, and said she would be prepared to undergo such a procedure again if necessary.

Cortical sensory evoked responses are now monitored routinely in parallel with the wake-up test. These provide a continuous record of spinal cord activity, but they do not allow assessment of motor function, and the technique is difficult to apply in patients with pre-existing neurological impairment.

Using the described method of anaesthesia in

40 cases, we have found the wake-up test very straightforward to apply during anterior spinal surgery and associated with a high degree of amnesia.

Department of Anaesthesia,
University Hospital,
Nottingham NG7 2UK.

P.A. Tomlinson
P.M. Yeoman
A.D. Jardine
J.K. Webb

A reply

Thank you for the opportunity to reply to Dr Schofield's illuminating comments to our article.

His 30-minute anticipation interval for wake-up requires considerable teamwork and experience. Surely anaesthetic equipment for sophisticated orthopaedic procedures needs upgrading. A peripheral nerve stimulator and an infusion pump are all that is required for the technique we described. The latter may be borrowed from most intensive care units.

It is to be hoped that the development of somatosensory evoked potential monitoring will eliminate the need for this disagreeable procedure.

Ealing Hospital,
Southall, UB1 3HW

Elizabeth G. Bradshaw

Biochemical changes associated with suxamethonium

Having read with interest the paper of Dr Laurence on the biochemical changes associated with the administration of suxamethonium (*Anaesthesia* 1985; **40:** 854–9), we would like to comment briefly on the findings in relation to potassium. No significant changes in the plasma potassium were found, and it was suggested that this might be accounted for by the absence of blood samples in the first 5 minutes after suxamethonium was given.

We have recently reviewed the literature on the potassium changes resulting from suxamethonium and have found that the evidence for the time course of these changes is indeed confusing. The many case reports of patients with abnormal sensitivity to suxamethonium as a result of burns, major trauma or spinal cord injury[1,2] suggest that the peak increase in potassium, which may be very large, is found within the first 5 minutes after the muscle relaxant is given, with a gradual return to base-line levels occurring in the following 30–60 minutes.

However, studies in patients with normal responses to suxamethonium[3,4] seem to indicate that although a much smaller rise in plasma potassium occurs, it is a more gradual and prolonged increase, with maximum potassium levels found between 10 and 60 minutes after administration of the muscle relaxant. If this is the case, then Dr Laurence may have missed the peak increase in potassium as blood samples were taken for only 20 minutes after suxamethonium. A recent study in dogs,[5] which examined the effect of beta-adrenoreceptor blockade on the potassium changes with suxamethonium, reiterates this point: the maximum change in non beta-blocked dogs was found 30–60 minutes after suxamethonium, compared with 60–90 minutes in the beta-blocked group.

We have undertaken a study in normal patients using an ion-selective electrode to record the potassium level continuously for 60 minutes after suxamethonium is given. We hope that the results from this study may help to clarify the time course of these events.

The Middlesex Hospital,
Mortimer Street,
London, W1N 8AA

H.F. Drake
W.A. Yanny

References

1. Viby-Mogensen J, Hanel HK, Hansen E, Graae J. Serum cholinesterase activity in burned patients II: Anaesthesia, suxamethonium and hyperkalaemia. *Acta Anaesthesiologica Scandinavica* 1975; **19:** 169–79.
2. Mazze RI, Escue HM, Houston JB. Hyperkalemia and cardiovascular collapse following administration of succinylcholine to the traumatized patient. *Anesthesiology* 1969; **31:** 540–7.
3. Bali IM, Dundee JW, Doggart JR. The source of increased plasma potassium following succinylcholine. *Anesthesia and Analgesia* 1975; **54:** 680–6.
4. Striker TW, Morrow AG. Effect of succinylcholine on the level of serum potassium in man. *Anesthesiology* 1968; **29:** 214–5.
5. McCammon RL, Stoelting RK. Exaggerated increases in serum potassium following succinylcholine in dogs with beta blockade. *Anesthesiology* 1984; **61:** 723–5.

A reply

Thank you for the opportunity to reply to Dr Drake and Dr Yanny. The literature on the subject of potassium changes and other side effects after suxamethonium administration does seem to contain much confusing information. The majority of reports, however, seem to look for, and to find, a small elevation of serum potassium within 5 minutes of administration. It was a little surprising, therefore, that neither of our published studies found any potassium changes in either control groups or alcuronium or dantrolene treatment groups, although Budd *et al.*,[1] in an earlier issue of the journal, found a similar lack of potassium response. Our main purpose was to report myoglobin changes, so we could not delay surgery for more than the 20 minutes of our study in order to look for late potassium changes. The few patients in whom we were able to sample beyond 20 minutes showed no potassium changes.

It is interesting to speculate on the possibility of two different mechanisms for potassium release. A subsequent study of serum myoglobin changes up to 2.5 hours after suxamethonium administration (during orthopaedic procedures with tourniquet control),[2] shows that serum myoglobin peaks 40 minutes after suxamethonium administration and then decays exponentially. Perhaps the slow potassium release (peak at 30–60 minutes) and myoglobin release (peak at 40 minutes) result from the same site of cellular damage due to suxamethonium administration. Myoglobin is water soluble and not bound to any subcellular structure; thus, it readily leaks out of a damaged cell. Muscle-cutting surgery (work in progress) results in myoglobin peaks at 2–3 days postoperatively, which suggests a totally different mechanism of release following this type of damage.

We look forward to future work, which will help to clarify the suxamethonium-induced serum potassium changes.

Royal Preston Hospital, A.S. LAURENCE
P.O. Box 66,
Sharoe Green Lane, Fulwood,
Preston PR2 4HT

References

1. BUDD A, SCOTT RFP, BLOGG CE, GOAT VA. Adverse effects of suxamethonium. Failure of prevention by atracurium or fazadinium. *Anaesthesia* 1985; **40:** 642–6.
2. NORRIS SH, LAURENCE AS, ROWLEY DI. Use of myoglobin assay to detect tourniquet ischaemia. *Journal of Bone and Joint Surgery* 1984; **67B:** 161–2 (Proceedings of British Orthopaedic Research Society and paper in preparation).

Formalin toxicity in hydatid liver disease

We read with interest the excellent paper written by Dr Aggarwal and Dr Garg (*Anaesthesia* 1983; **38:** 662).

We have experienced similar episodes. However, the outcome in our four cases was not fatal, although the patients had severe manifestations of formalin toxicity. The favourable outcome was probably due to the fact that concentration of formalin was far less than 100 percent and 25 percent, which were used in the two patients presented by Dr Aggarwal and Dr Garg. In addition, we consider the amount of solution (> 900 ml) to be excessive.

When formalin is used, the following preventive measures should be taken. The concentration of formalin should not exceed 2 percent and the volume should not exceed 200–300 ml. If the cyst fluid contains blood or bile, formalin should not be used, because communications between the cyst and blood vessels or bile ducts exist.[1] A wet pack with normal saline should be used to protect abdominal viscera from formalin contact before the formalin packs are put around the cyst.

Many authors believe that formalin, in concentrations effective against scolices, is toxic to the host as well and, therefore, condemn it as a treatment for hydatid cysts.[2,3] Thus, for the last few years, we have used 0.5 percent silver nitrate solution, which is not toxic to the host and leads to the death of scolices.[4] An additional useful feature of silver nitrate is its low viscosity, so that the solution may be poured into the pericystic cavity to enter all crevices and interstices in the cyst walls. However, we consider that proper protection of the surgical field and safe aspiration of the cyst fluid by means of a large bore trocar, connected to strong suction are simple, logical and safe steps for the removal of the parasite.

The ancient aphorism of Hippocrates 'To benefit and not to harm' must be one of the inviolable principles in every day surgical practice.

2nd Surgical Unit, J. PAPADIMITRIOU
Athens University,
76 Vas Sophias Avenue,
Athens (115 21) Greece.

Department of Anaesthesia L. PAPADIMITRIOU
Evangelismos Hospital,
Athens (115 21) Greece

References

1. PAPADIMITRIOU K, TSIFTIS D, TOUNTAS C. Hydatid cyst of the liver ruptured into the biliary tract. *Current Surgery* 1983; **40:** 339–46.
2. HANKINS J, DUTZ W, KOHOUT E. Surgical treatment of ruptured and unruptured hydatid cysts of the lung. *Annals of Surgery* 1968; **167:** 336–41.
3. PEREZ FONTANA V. El formol y el clorwro de sodio en el tratamiento del quiste hidatico. *Archivos Internacionales de la Hidatidosis* 1961; **20:** 315–9.
4. SCHWABE CW. Lateral echinococcus infection in laboratory animals. *Bulletin of the World Health Organization* 1968; **39:** 126–7.

A reply

Thank you very much for the opportunity to reply to J. Papadimitriou and L. Papadimitriou, with whom we fully agree that the concentration, volume and duration of contact of formalin used in patients with hydatid liver disease is of the utmost importance. The concentration and volume of formalin used was excessive in our first case. The purpose of our report of these two cases was to distinguish the signs of anaphylaxis from the severe acidosis caused by formic acid in formalin toxicity. The precautionary measures and treatment of formalin toxicity was discussed in our article. Nowadays, many surgeons have started to use either a solution of 3 percent silver nitrate or hypertonic saline 5 percent or cetrimide.

Department of Anaesthesia, A.R. AGGARWAL
Sir Ganga Ram Hospital, R.L. GARG
Rajinder Nagar,
New Delhi-110060, India.

High frequency jet ventilation through a Robertshaw double lumen tube

There have been reports of the use of high frequency jet ventilation during pulmonary surgery delivered via tracheal tubes to both lungs throughout surgery, or delivered via a bronchial tube in one lung only. There is some evidence that high frequency ventilation may reduce the amount of intrapulmonary shunting[1] compared with conventional intermittent positive pressure ventilation of one lung.

This is a report of the use of high frequency jet ventilation, delivered via a standard Robertshaw double lumen tube during pulmonary surgery (lobectomy, pneumonectomy, sleeve resection). A fine catheter was passed down each lumen of the double lumen tube, to a point level with the tracheal cuff. The two catheters were connected together with a Y-connector, which was then connected to the Acutronic high frequency jet ventilator. High frequency jet ventilation at rates of 100–150 breaths/minute was delivered via this system. The catheter size was selected to give an 'inspiratory jet port' to 'expiratory exhaust port' ratio of 1:6. Both lungs could be ventilated with a switch to one lung when required, by clamping one catheter.

Following preliminary work using dummy lungs, a small series of patients were ventilated by this method during pulmonary surgery. Informed consent was obtained from all patients.

Ten patients received high frequency jet ventilation at rates of 100–150 breaths/minute. All were ventilated to normocapnia (range $Pa\text{CO}_2$ 4.5–5.3 kPa) without added positive end expiratory pressure. High frequency jet ventilation was delivered via the catheters to both lungs initially, switching to one lung when required by the demands of surgery. Normocapnia and adequate arterial oxygenation were maintained throughout the period of one lung ventilation. Re-expansion of the unventilated lung was achieved by unclamping the catheter to that side, switching the jet ventilator to manual mode and delivering 5–10 breaths of 1–2 seconds duration.

The shunt fraction was estimated 20 minutes after the start of one lung ventilation, by standard methods.[2] (Central venous blood was used as an approximation to mixed venous.) The mean estimate for shunt fraction was 24.2 percent (range 15–35 percent).

For comparison, the shunt fraction was measured in ten similar patients undergoing pulmonary surgery, receiving conventional intermittent positive pressure ventilation during one lung ventilation. A volume preset Blease pulmoflator was used without added positive end expiratory pressure. Normocapnia was maintained throughout (range $Pa\text{CO}_2$ 4.4–5.3 kPa). The mean estimate for shunt fraction after 20 minutes of one lung ventilation was 25.1 percent (range 20–32 percent).

In this small series of patients, no improvement in shunt fraction was seen during one lung ventilation with high frequency jet ventilation, compared with that during conventional ventilation. However, the surgical conditions were noted to be excellent, with very little mediastinal movement. The advantages of a double lumen tube in isolating suppuration and haemorrhage were maintained when delivering high frequency jet ventilation by this method. The method probably warrants further investigation with measurement of mean and peak airway pressures as well as shunt fraction. There may prove to be advantages in central haemodynamics[3] if low mean airway pressures can be maintained.

Department of Anaesthesia,
Hope Hospital,
Salford, M6 8HD.

C.J. Mason

References

1. El-Baz N, El-Ganzouri A, Ivanovich AD, Faber LP, Kittle CF, Jensik R. One-lung high-frequency positive-pressure ventilation during lung surgery. *Anesthesia and Analgesia* 1982; **61:** 180–1.
2. Fiser WP, Friday CD, Read RC. Changes in arterial oxygenation and pulmonary shunt during thoracotomy with endobronchial anesthesia. *Journal of Thoracic and Cardiovascular Surgery* 1982; **83:** 523–31.
3. Peltola K. Central haemodynamics and oxygenation during thoracic anaesthesia. *Acta Anaesthesiologica Scandinavica* 1983; Supplementum 77, 27.

Hallucinations after oral lorazepam in children

My family and I recently returned to Riyadh from North America. My two children were jet-lagged and unable to sleep. Lorazepam (Ativan) was given to them by the writer as a sedative, with unfortunate results. The severity of their resulting visual hallucinations was most alarming, and emphasised the possibility of this side effect when using lorazepam in children.

The two children, aged 6 and 8 years, were given lorazepam in doses of 0.083 mg/kg and 0.1 mg/kg respectively, somewhat in excess of the oral dose of 0.05 mg/kg recommended by Mundeleer.[1] A variety of visual hallucinations accompanied by emotional lability commenced in both children about three quarters of an hour after ingestion of the tablets and lasted for 4–5 hours, not, unfortunately, followed by amnesia for the event.

The use of lorazepam as premedication in children has been the subject of recent studies.[1–3] Peters *et al.*,[2] used lorazepam in the recommended oral dose and reported three instances (2.6 percent) of hallucinations in their series of 112 children. This high incidence of an undesirable side effect, in conjunction with the severe reaction seen in my children, suggests caution in the use of lorazepam as a sedative or premedicant in children.

Department of Anaesthetics, A.A. VAN DEN BERG
Riyadh Armed Forces Hospital,
P.O. Box 7897,
Riyadh 11159,
Saudi Arabia.

References

1. MUNDELEER P. Child premedication per os with lorazepam. *Acta Anaesthesiologica Belgica* 1980; **31** (Suppl.): 187–93.
2. PETERS CC, BRUNTON JT. Comparative study of lorazepam and trimeprazine for oral premedication in paediatric anaesthesia. *British Journal of Anaesthesia* 1982; **54**: 623–7.
3. BURTLES R, ASTLEY B. Lorazepam in children. A double-blind trial comparing lorazepam, diazepam, trimeprazine and placebo. *British Journal of Anaesthesia* 1983; **55**: 275–8.

Puncture of the ascending aorta—a complication of subclavian venous cannulation

The report by Dr Hirsch and Dr Robinson[1] prompts us to record a similar complication of subclavian venous cannulation in a patient with acute renal failure.

A 32-year-old man suffered multiple rib fractures after a road accident, together with a central fracture–dislocation of his hip and a ruptured spleen; the latter was removed at exploratory laparotomy. He developed respiratory failure and septic shock postoperatively and underwent mechanical ventilation of his lungs. A left-sided pneumothorax necessitated the insertion of a left intercostal underwater-seal drain. Twenty-eight days after the incident, he developed acute renal failure and was transferred to the intensive therapy unit of this hospital for haemodialysis.

On admission he was conscious; he had been breathing spontaneously via a tracheostomy for 12 hours, but was jaundiced with hepatomegaly, ascites and gross abdominal distension. A chest X ray showed bilateral, diffuse pulmonary infiltrates and a prominently raised diaphragm on both sides. The left-sided pneumothorax had almost completely resolved, but the left intercostal drain was still in place.

A haemodialysis line of the Uldall type was inserted into the right subclavian vein without difficulty, and the patient had 4 hours of haemodialysis. Three hours later, an attempt was made to cannulate the left subclavian vein for the administration of 50 percent dextrose and central venous pressure monitoring, using the intraclavicular approach.

The usual precautions were followed, including the use of a 20° head-down tilt. An 8-cm long, 12-gauge needle, standard in the Vygon Nutricath 'S' pack, was used. It was thought that the vein had been cannulated on two occasions, but it was impossible to thread the catheter and the procedure was abandoned. The patient's systolic blood pressure decreased to 50 mmHg (direct intra-arterial recording) within a few minutes. This hypotension rapidly responded to two units of human plasma protein fraction and two units of albumin 20 percent, but over a further 10 minutes his condition deteriorated, with a falling blood pressure and a central venous pressure, measured via the Uldall line, of +30 cmH_2O. Resuscitative measures included external cardiac massage, manual ventilation of the lungs with 100 percent oxygen, aspiration of the left intercostal drain for air or blood, as well as the insertion of a 16-gauge needle attached to a fluid-filled syringe at two sites in the left hemithorax to exclude a tension pneumothorax or haemothorax.

Pericardial tamponade was certainly considered and two attempts were made to aspirate the pericardial sac by the sub-xiphisternal route with a 4.5 cm and then a 5.7 cm needle. Four hundred and sixty ml of straw-coloured fluid was obtained, but neither blood nor air was aspirated. By this time, despite further volume replacement and pharmacological efforts to restore the circulation, acute circulatory insufficiency had developed and the pupils were fixed and dilated.

Postmortem examination revealed a haemopericardium and two puncture sites in the ascending aorta within 2 cm of the aortic valve root. There was no sign of a tension pneumothorax. The mediastinum had been displaced in a cephalad direction, secondary to the marked abdominal distension which had been caused by the combination of ascites and severe bowel distension.

For the past decade, all central venous lines have been passed in this unit exclusively via the percutaneous infraclavicular approach to the subclavian vein without any previous major complication other than a pneumothorax rate of less than 0.5 percent. There are several important features of this case which we feel deserve wider discussion. Firstly, previous reports of pericardial tamponade associated with central venous cannulation have been secondary to perforation of the great veins, atrium or ventricle by the catheter tip, resulting in hydromediastinum which later caused extrapericardial tamponade, or direct intrapericardial tamponade due to the infusion of intravenous fluids.[2–4] Most cases have been fatal. We believe this to be the only report of aortic puncture within the pericardial reflection by a needle used to initiate central venous cannulation.

The markedly elevated diaphragm and reduced intrathoracic volume secondary to gross abdominal distension, ascites and hepatomegaly, were noted on the chest X ray prior to attempted subclavian vein cannulation, but their implications regarding distortion of mediastinal anatomy were not fully appreciated. In patients who have a cephalad displacement of the mediastinum and great vessels, faith in the classical anatomical landmarks needs to be tempered with great caution, especially when a 20–25° head-down tilt is used routinely,[5] since this exacerbates the effect of any abnormality.

Marked upward displacement of the inferior pericardial surface accounted for the failure to aspirate blood from the pericardial sac by the sub-xiphisternal route in this case. Most authors suggest this is the safest route for pericardiocentesis,[2,6] since the alternative parasternal approach has a higher incidence of dysrhythmias, cardiac puncture and laceration of the anterior descending coronary artery.[7] Sub-xiphoid pericardiostomy or window has been described as an emergency measure, as well as limited thoracotomy through the 4th or 5th left intercostal space,[6] although the clinician who has no immediate access to cardiothoracic surgical expertise must exercise careful judgement before undertaking such heroic procedures.

This case suggests that, in the presence of marked abdominal distension from any cause, including pregnancy, percutaneous subclavian cannulation particularly on the left side, is a hazardous procedure and should be undertaken with great caution. It may also be wiser practice to avoid long, large-bore needles and catheter-through-needle devices such as the one used in this case, and to limit venepuncture to shorter, small-gauge needles with a subsequent Seldinger wire technique, although this too has complications.

General Intensive Therapy Unit, D. Childs
Royal Liverpool Hospital, R.G. Wilkes
Prescot Street,
Liverpool L7 8XP.

References

1. Hirsch NP, Robinson PN. Pulmonary artery puncture following subclavian venous cannulation. *Anaesthesia* 1984; **39**: 727–8.
2. Geis WP, Johnson CF, Zajtchuk R, Kittle CF. Extra-pericardial (mediastinal) cardiac tamponade. *Archives of Surgery* 1970; **100**: 305–6.
3. Bone DK, Maddrey WC, Eagan J, Cameron JL. Cardiac tamponade. A fatal complication of central venous catheterization. *Archives of Surgery* 1973; **106**: 868–70.
4. Csanky-Treels JC. Hazards of central venous pressure monitoring. *Anaesthesia* 1978; **33**: 172–7.
5. Rosen M, Latto IP, Ng WS. *Handbook of percutaneous central venous catheterisation*. Philadelphia: W.B. Saunders, 1981.
6. Peters RM. Trauma to the chest wall, pleura and thoracic viscera in: Shields TW ed. *General thoracic surgery* (2nd edn). Philadelphia: Lea and Febriger 1983; 387–8.
7. Cassell P, Cullum P. The management of cardiac tamponade. Drainage of pericardial effusions. *British Journal of Surgery* 1967; **54**: 620–6.

Difficult tracheal intubation

In reply to Dr Zuck's letter (*Anaesthesia*, 1985; **40**: 1016) the measurements on the lateral X ray of our patient (in the neutral position) were: posterior mandibular depth 2.6 cm and effective mandibular length 10.6 cm, achieving a ratio of 4:1. The atlanto-occipital gap was 8 mm. According to White and Kander,[1] this ratio should indicate easy intubation in the absence of other factors. We described prominent asymmetrical teeth, although these did not obscure the view. Substitution of our measurements into Dr Cormack's derived equation[2] which relates the posterior mandibular depth to atlanto-occipital gap, provided further indication that intubation should not have been difficult (personal communication).

Our case demonstrates fallibility of two radiological methods, both carried out in retrospect, for the detection of difficult intubation. We await with interest Dr Zuck's findings relating cervical spine convexity to laryngeal position in the coronal plane.

There is a need for a simple pre-operative screening test, to alert us to possible difficulty and whether to undertake prospective radiological measurements. It seems that the predictive reliability of these has yet to be established.

Department of Anaesthetics, I.D. Levack
Royal Infirmary, A.H.B. Masson
Edinburgh.

References

1. White A, Kander PL. Anatomical factors in difficult direct laryngoscopy. *British Journal of Anaesthesia* 1975; **47**: 468–74.
2. Evans R, Cormack RS. Difficult intubation. *Anaesthesia Points West* 1984; **17**: 79–80.

Difficult tracheal intubation in obstetrics

The study by Dr Lyons (*Anaesthesia* 1985; **40**: 759–63) is important and I am sorry if my comments seemed to him[1] critical. His strategy may help to prevent maternal deaths; certainly we all hope so, because it would be nice if the solution were as simple as that. Unfortunately, the data he cites are far from proving his point.

The triennial report for 1976–78, to which he refers, found 20 deaths in about 120 000 anaesthetics in the United Kingdom; a mortality of about 1 in 6000. His own study had no deaths in 2400 cases. Thus, no calculation is needed to see that the facts are consistent with his regimen giving a greater mortality than the national average. To prove that it is better than average, one has to show zero deaths in at least 29 000 anaesthetics—this would make $p = 0.05$ by the simple Chi squared test as described, for example, by Sykes and Vickers[2] (Fisher's exact test leads to a similar conclusion, but the logical defect in the final step of this test[3] is not resolved, as yet).

Training. The factors which may complicate tracheal intubation in obstetric anaesthesia are well known, but should not cause failure. Simple ways of coping with mammamegaly, for example, have been known for ages. The strongest reason for trying to reduce the number of failures is that the only certain way of preventing Mendelson's syndrome is a cuffed tube in the trachea. If Dr Lyons is not convinced by us, can I suggest that he put the following questions to all junior staff who apply to join his department.

What anatomical features are the main cause of unexpected difficult intubation in patients with no neck pathology?

Such patients can often be intubated without great difficulty, by what method?

How often have you practised this method?

The right answers would, I daresay, be given by Dr Lyon's trainees, but he will find that others often give quite the wrong answers, even senior registrars from teaching hospitals. This is a gap in our present training, due partly to the lack of a useful section on it in
textbooks.

Anxiety. Dr Lyons believes that anxiety is
important factor in causing failed intubation; we a
entirely and that is the whole point of our dr
Difficult intubation is rare, so a registrar who is unlu
enough to meet this in maternity will have had l
experience of handling it. In fact, he may never h
seen it before, so panic is likely. Our solution i
simulate the difficult case on routine lists and prac
the blind intubation method. Then, if the trainee m
a real case, he will be familiar with its appearance
its management, so there should be no great alar

Is it right to organise increasingly costly, labori
and complex antacid regimens, without first carr
out this much simpler measure? We would welcome
Lyons' comments.

Northwick Park Hospital, R.S. CORM
Harrow, HA1 3UJ.

References

1. LYONS G, MACDONALD R. Difficult intubation in obstet
Anaesthesia 1985; **40:** 1016.
2. SYKES MK, VICKERS MD. *Principles of measurement*
anaesthetists. Oxford: Blackwell, 1970: 284–6.
3. CORMACK RS. Anomalies in Fisher's Exact Test. *Journ*
the Royal Statistical Society (A) 1984; **147:** 455.
4. CORMACK RS, LEHANE J. Difficult tracheal intubatio
obstetrics. *Anaesthesia* 1984; **39:** 1105–11.

Urban hypothermia

Dr N.V. Fergusson (*Anaesthesia* 1985; **40:** 651–4) should be congratulated on the successful resuscitation of his case of hypothermia, and it is encouraging to read another case report suggesting that active, invasive rewarming is not an absolute necessity for the successful resuscitation from ventricular fibrillation in hypothermia. It was personally pleasing also to see that part of the rewarming technique included the use of heated humidified ventilator gases (airway warming).

However, the title Urban hypothermia is peculiar, not least since the case occurred under circumstances more likely to be found in the country. The history of the case suggests that hypothermia was caused by the rate of heat loss being so great that it overwhelmed the body's heat production: it was of the immersion type.[1] In the reported case, the rate of heat loss would be increased by drug and alcohol induced vasodilatation plus soaked clothing in a very cold environment, while the rate of heat production would be impaired by the alcohol. The history certainly does not match the exhaustion type of hypothermia which occurs among climbers. The other common type of accidental hypothermia is the subchronic type usual among the elderly, in which the person is exposed to cold stress for a prolonged period, days or weeks, before becoming clinically hypothermic. The fluid shifts which o
during prolonged exposure to cold cause probl
during rewarming.[2] If the term urban hypotherm
used, it should, in my opinion, be reserved for
subchronic type of hypothermia.

Department of Anaesthetics, E.L. LL
Princess Margaret Rose Hospital,
Fairmilehead,
Edinburgh.

References

1. LLOYD EL. Treatment of accidental hypothermia. *Br*
Medical Journal 1979; **1:** 413–4.
2. LLOYD EL. *Hypothermia and Cold Stress.* London: Cr
Helm. 1986 (in press).

A reply

Thank you for sending me Dr E.C. Lloyd's letter.

The case described does indeed best fit with
immersion type of hypothermia within the classificat
of immersion exhaustion and subchronic types. The
Urban hypothermia was chosen to draw attention to

point that the case occurred in an urban environment and that immersion and exhaustion types of hypothermia may be seen in urban areas.

Royal Berkshire Hospital,
Reading,
Berkshire, RG1 5AN.

N.V. Fergusson

Epidural test dose

Dr Kumar and his colleagues (*Anaesthesia* 1985; **40:** 1023) state in their letter that a dose of 1.5–1.6 ml 0.5 percent plain isobaric bupivacaine injected intrathecally produces a block up to T_{12} within 3 minutes, and go on to recommend that this would be a suitable test dose to exclude intrathecal placement of the epidural catheter.

My experience of spinal anaesthesia in over 100 patients using 0.5 percent plain isobaric bupivacaine, suggests that there is a marked variation in onset time which may be between 2 and 15 minutes. A dose of 3 ml injected intrathecally into pregnant women may indeed produce an extensive block, but I do not consider that 1.5 ml 0.5 percent bupivacaine is a suitable test dose. Five percent lignocaine produces a rapid block when used for spinal anaesthesia and I therefore agree with Dr Casey (*Anaesthesia* 1985; **40:** 597) that 1.5–2.0 ml 5 percent lignocaine would constitute an effective test dose and is worth consideration. The addition of 0.015 mg adrenaline would help detect intravascular placement.

Whittington Hospital,
Highgate Hill,
London N19 5NF.

S. Mallaiah

Eye to eye with Murphy's law

We recently encountered an unusual problem in our intensive care unit. A 27-year-old female was found to require high inflation pressures for mechanical ventilation of her lungs and she produced copious amounts of purulent sputum. We elected to employ a flexible fibreoptic bronchoscope to examine her tracheobronchial tree.

The well lubricated instrument was passed without difficulty through the tracheal tube, and the carina and right-side bronchi were readily visualised. However, attempted withdrawal of the bronchoscope, to examine the left side, met with significant resistance. The bronchoscope could be advanced but not withdrawn. For fear of damage to patient or instrument, the cuff of the tracheal tube was deflated and both tube and bronchoscope were removed together, revealing the cause of the problem (Fig. 1).

The hole in the bevel of a tracheal tube, or Murphy's eye,[2] was described to allow gas to pass should the bevel of the tube be occluded by the wall of the trachea or by any other obstruction. Fortunately, in this instance, while complicating a normally simple procedure, no harm came to either patient or instrument.

Departments of Anaesthetics
and Thoracic Surgery,
Wentworth Hospital,
Private Bag Jacobs 4026,
Durban, South Africa.

R.G. MacGillivray
J.A. Odell

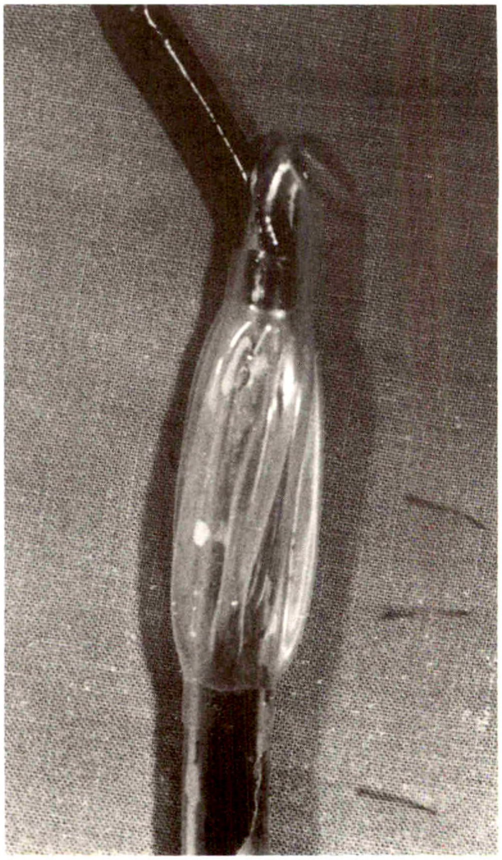
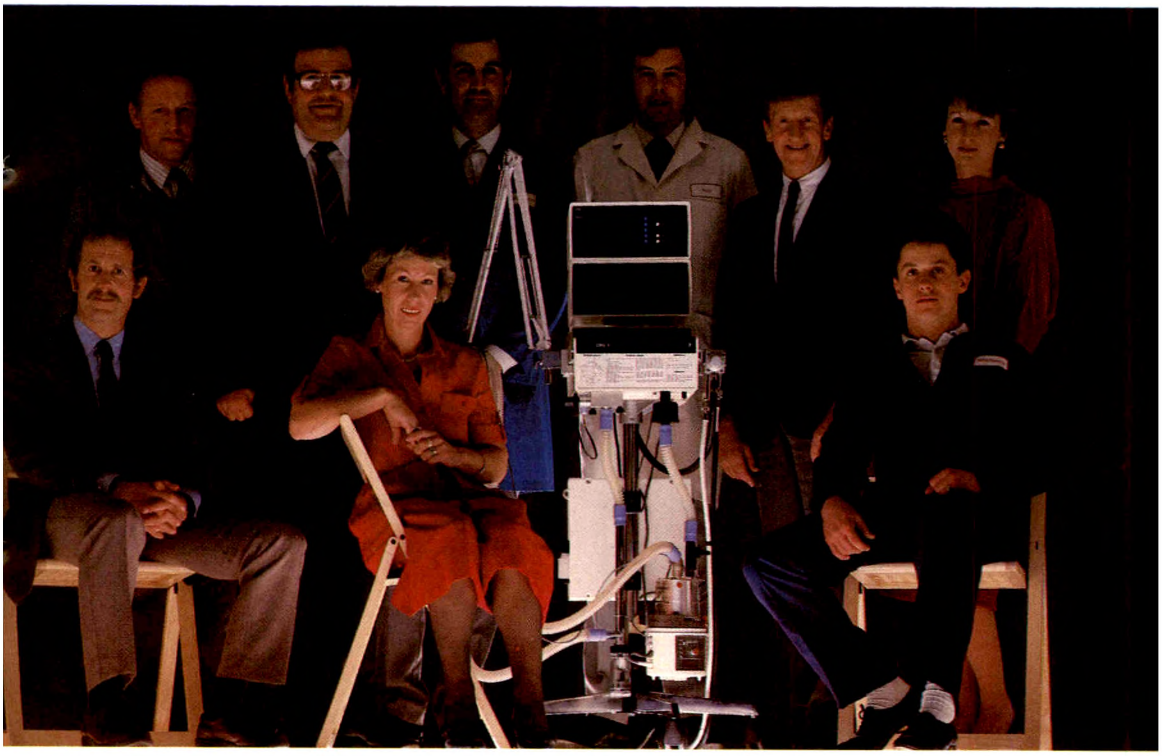


Fig. 1. Fibreoptic bronchoscope emerging from Murphy's eye of tracheal tube.

References

1. Bloch A. Murphy's Law—'If anything can go wrong, it will'. In *Murphy's law—and other reasons why things go wrong*. Los Angeles: Price, Stern & Sloan, 1977.
2. Murphy FJ. Two improved intratracheal catheters. *Anesthesia and Analgesia* 1941; **20:** 102–5.



At Ohmeda the critical difference is people.

So we've established centres of excellence to ensure that every sector of our company is run by dedicated experts. One such centre is devoted to critical care.

At this centre our specialist team has designed, produced and tested our complete range of critical care equipment.

A totally integrated range that encompasses first line therapy with the unique CPU1 ventilator; monitoring, oximetry and suction equipment and, of course, all the ancillaries such as face masks and patient circuits.

It's a highly flexible, reliable and comprehensive range that provides complete respiratory support for adults and paediatrics plus a full range of neo natal equipment including a resusitation unit, infant warmers, intensive care and transport incubators.

Specify excellence, specify Ohmeda.

SPECIALIST EQUIPMENT FOR SPECIALIST PEOPLE

Ohmeda

Ohmeda
Elizabeth Way Harlow Essex CM19 5AB England
0279 29692 Telex 81497

THE
EUROPEAN
DIPLOMA
IN
ANAESTHESIOLOGY

In 1984, the European Academy of Anaesthesiology introduced this postgraduate examination which is of interest to anaesthesiologists throughout Europe. It is a two-part examination, Part I being multiple choice questions (MCQ) and Part II an oral examination. The examination is being conducted in English, French, German, Italian and Spanish.

The intentions of the European Academy are that the Diploma will:

- provide a European title of distinction that will be recognised as evidence of a high standard of training and distinction.
- assist in the raising of standards of anaesthesiology throughout Europe.
- be adopted by some European countries as a criterion of specialist achievement.
- facilitate the movement of anaesthesiologists in Europe, especially in the countries of the EEC.

The 1986 Part I (MCQ) Examination will be held on **Thursday, 18th September** in Strasbourg, Oslo and Rome. The Examination Regulations and Calendar, giving the criteria for entry, fees and other details, are available in any of the five languages listed above and may be obtained from:

The Examination Secretary, European Academy of Anaesthesiology, 9 Bedford Square, London WC1B 3RA
(Tel: 01 631 1650).

The end of the crystalloid era?

There is much that is interesting and challenging in the paper by Twigley and Hillman (*Anaesthesia* 1985; **40:** 860–71) who make a plea for more account to be taken of colloid solutions which have oncotically active solutes. The authors treat the modified gelatins as though they were identical; this is not so. Haemaccel (polygeline) contains more than ten times the concentration of both calcium and potassium that is found in Gelofusine and all the documented accounts of histamine release have applied to Haemaccel. This so-called 'relative hypovolaemia' resulting from sympathetic blockade in epidural analgesia is particularly likely to be associated with anaphylactoid reactions to rapid infusion of Haemaccel,[1,2] and it should not be used for this purpose.

Is it not time that British anaesthetists started to use the increased supplies of 4.5 percent albumin promised by the Blood Products Laboratory in 1984?[3] The plasma is a by-product of fractionation of whole blood for other purposes and its cost is therefore not a valid reason to choose a synthetic substitute. The preparation has been unjustly condemned in the United Kingdom, as a result of the report from Seattle[4,5] of kallikrein activity in plasma protein fraction due to heat applied in its preparation. Lane[3] contends that the UK product has a long record of use, uncomplicated by reports of hypotensive reactions and Factor XII fragments (prekallikrein activators) are usually undetectable.

Shackleton Department of Anaesthetics,
Southampton General Hospital,
Southampton, SO 4XY.

P.J. Horsey

References

1. Lund N. Anaphylactoid reaction to infusion of polygelatin (Haemaccel). A study in pregnant women. *Anaesthesia* 1980; **35:** 655–9.
2. Freeman MK. Fatal reaction to Haemaccel. *Anaesthesia* 1979; **34:** 341–3.
3. Lane RS, Vallet L. Human albumin and plasma protein fraction. *Lancet* 1984; **1:** 1245–6.
4. Alving BM, Hojima Y, Pisano JJ, Mason BL, Buckingham RE, Mozen MM, Finlayson JS. Hypotension associated with prekallikrein activator. (Hageman factor fragments) in plasma protein fraction. *New England Journal of Medicine* 1978; **299:** 66–70.
5. Colman RW. Paradoxical hypotension after volume expansion with plasma protein fraction. *New England Journal of Medicine* 1978; **299:** 97–8.

Here are a few comments concerning Twigley and Hillman's review. The authors' message seemed to be that fluid restriction during the day of operation, in moderate surgery, and intravenous cannulae and infusion are unnecessary and that, if hypovolaemia occurs, volume should be replaced with colloid solutions. The colloid and crystalloid discussion has gone on for many years and it is surprising that yet another article tries to swing the pendulum back in favour of 'colloid only' therapy. Surely, if there are good arguments on both sides, the truth must lie somewhere in between.

First of all, it is totally unacceptable to suggest that patients need not have an intravenous cannula and infusion during and after operation, apart from minor procedures. This would be a large step backwards in the practice of anaesthesia. It is difficult to understand that an indwelling cannula gives rise to pain, infection and thrombophlebitis after 24 hours; this is not the case in Sweden. My views are based on clinical observation and not on radio-isotope studies. One thing is certain and that is that if the only fluids given during larger procedures are those required to replace blood losses, then the patient will show all the signs of hypovolaemia in the postoperative period.

There are many reasons for fluid losses including evaporation, transudation and shifts into the interstitial compartment. Losses to the outside need to be replaced: the nature of this loss, mostly low in sodium, with some degree of protein loss indicates that a dextrose/saline type of solution should be suitable, with extra protein should transudation losses be large.

The losses due to shifts of fluid between the compartments are somewhat more complicated. These cannot be regarded as loss since fluid remains in the the tissues and is available to the circulation later. The argument that it is illogical to replace this deficit with solutions, 75 percent of which, pass into the extracellular compartment is a logical one. In medical practice, however, it is not unusual that, what is logical in theory, does not apply in practice.

It has been shown in connexion with blood loss replacement[1] that if colloid is used instead of crystalloid, together with erythrocytes, then although twice as much crystalloid as colloid is required to maintain a steady wedge pressure, more problems arise in the colloid group in the postoperative period, since the other group can increase urine output. Once in, colloids are more difficult to extract.

It is possible that there is a tendency to overfill patients in Sweden by following rather extreme crystalloid regimens, but there seems to be a trend towards a compromise with the use of a regimen, including both colloid as dextran 70, and a dextrose/saline solution in somewhat lesser amounts. The introduction of the pretreatment of patients with a dextran hapten, consisting of a solution of 1000 dalton dextran molecules, has reduced the incidence of allergic reactions to dextran to zero. The use of dextran solution also has the advantage that the incidence of deep vein thrombosis is greatly reduced.

Where fluid shifts are expected to be large, we usually introduce a central venous catheter to facilitate monitoring of the treatment. Swan-Ganz catheters are reserved for complicated cases. The important thing is to ensure that fluid excesses incurred during the day of operation are retrieved in the postoperative period through fluid restriction and diuretic therapy if necessary.

In suggesting a regimen of fluid restriction and colloid-based therapy, I consider that Twigley and Hillman are treading on illogical dangerous ground.

Lasarettet,
591 85 Motala,
Sweden.

P. Cox

Reference

1. Virgilio RW, Rice CL, Smith DE, James DR, Zarins CK, Hobelmann CF, Peters RM. Crystalloid vs. colloid resuscitation: is one better? *Surgery* 1979; **85:** 129–39.

A reply

Thank you for the opportunity to reply to both these letters.

Dr Horsey is correct with his suggestion that there are more reports about Haemaccel and histamine release than after other modified gelatins. This impression may be because it is based on relatively few case reports and Haemaccel is by far the most commonly used modified gelatin in clinical practice. However, I disagree with Dr Horsey's conclusions that Haemaccel is particularly associated with anaphylactoid reactions during epidural analgesia and therefore that it should not be used for this purpose. The evidence for this is based on two reports with a total of seven cases.[1,2] The first case was almost certainly related to his history of severe allergic asthma rather than the epidural,[1] and the second report included six cases, two of whom had an epidural, one had an epidural and general anaesthetic and three had general anaesthesia. The incidence of anaphylactoid reactions with all of the colloids is extremely rare.[3]

Our message has been somewhat oversimplified and misunderstood by Dr Cox. We suggest no fluid where it is not needed, relatively less fluid where that is all that is required and the correct fluid when treating hypovolaemia. The problem of pre-operative fluid balance is difficult, as Dr Cox points out. However, it has been made a bit more difficult than is perhaps necessary, and it is complicated further by suggestions that, because certain fluid regimens have worked in the past, (that is, patients have on the whole survived them) then they must be ideal. Clinical observations are subject to the same criticisms as all observations unless they are rigorously tested. If blood losses are adequately replaced in Dr Cox's hypothetical patients, then it is difficult to understand why they should still show all the signs of hypovolaemia; it is very unlikely that it would be due to inadequate crystalloid replacement of the interstitial space. Indeed, in the reference quoted in Dr Cox's letter, both crystalloids and colloid were titrated against wedge pressure. It is logical to titrate a colloid, most of which remains in the intravascular space, against wedge pressure, but it is illogical to titrate crystalloid solution, most of which is distributed to the interstitial space against a measurement which relates to the intravascular space. The problem of extracting colloids, once they are in, is overcome by giving the correct amount in the first place. This involves titrating the colloid against the many measurements used to assess intravascular volume. The criticism by Dr Cox of our suggested policy of using relatively less crystalloid and a more rational approach to hypovolaemia seems to be negated by his own observation that there is a recent trend in Sweden also to use less extreme crystalloid regimens and more hyponatraemic solutions together with colloid, in the form of Dextran 70.

The Intensive Care Unit,
The Liverpool Hospital,
Liverpool, NSW, 2170,
Australia.

K. Hillman

References

1. Lund N. Anaphylactoid reaction to infusion of polygelatin (Haemaccel). A study in pregnant women. *Anaesthesia* 1980; **35:** 655–9.
2. Freeman MK. Fatal reaction to Haemaccel. *Anaesthesia* 1979; **34:** 341–3.
3. Ring J, Messmer K. Incidence and severity of anaphylactoid reactions to colloid volume substitutes. *Lancet* 1977; **1:** 466–9.

Transient loss of consciousness after therapeutic epidural injection

The controversy as to who called attention to the above stated problem caused me to chuckle and I enjoyed the one-upmanship involved (*Anaesthesia* 1985; **40:** 824–5).

In addition to this problem, the possibility of even more serious consequences was cited 30 years ago,[1] where the following (paraphrased) was stated about the subject.

'Not infrequently the anesthesiologist is requested to perform pressure caudal injections for sciatic or back pain. This entails the rapid injection of 50–90 ml of solution into the caudal canal.

It is common for the referring physician to manipulate the patient's legs and back after the injection of the solution. This is usually performed with much vigour. Because the manipulation of the back is attended with pain, the patient must receive either a regional anesthetic or a general anesthetic. Following regional anesthesia, we have observed convulsions not due to systemic toxic reaction. Following general anesthesia and this technique, Callahan, McConville, and Goss (personal communication) have observed 8 cases of retinal hemorrhage.'

Department of Anesthesiology,
University of Washington,
School of Medicine,
Seattle, Washington 98195
USA.
D.C. MOORE

Reference

1. MOORE DC. *Complications of regional anesthesia.* Illinois USA: Thomas, Springfield, 1955, 231–2.

Labels for drug ampoules

Dr Rendell-Baker's interesting letter (*Anaesthesia* 1985; **40:** 912–3) about the syringe labelling only touched on the labelling of ampoules, although it might be thought that this is a matter in need of far more attention.

It is obvious that no thought has been given to the user's needs in relation to small ampoules. Two random examples, which are probably no worse than many others, are labelled thus: 'Cyclimorph 10 containing Morph tart 10 mg Cyliz tart 50 mg Use S/C I/M or I/V CD POM Calmic Lot 57856', in orange and 'Atropine sulphate injection BP 600 mcg in 1 ml for S.C. I.M. or I.V. inj Evans Medical Ltd Batch B088 Use before March 1987' in blue, both on clear glass. The single, truly useful word 'Atropine' has to be read against the background of the wording on the far side of the ampoule. The lettering is about 1 mm high. Keen eyes must be at their limits here and the tired or old must be beyond them.

Labellers should use the minimum of words and the one or two clinically vital words should be large and, most importantly, printed on a contrasting background. What about 'Cyclimorph 10' and 'Atropine 600 mcg' only? I dare say other interests might rightfully require additional wording, but this must not be allowed to reduce the drug name to the same size as the batch number and thus, near illegibility.

Paper labels are, on the whole, superior to printing on glass. Small print is for lawyers, not doctors. Might not the Association produce some guidelines for manufacturers?

Arrowe Park Hospital,
Arrowe Park Road,
Upton, Wirral, Merseyside L49 5PE
B.P. GURATSKY

Nasotracheal intubation

The letter from Dr Boysen (*Anaesthesia* 1985; **40:** 1024) about the potential danger of tracheal tube occlusion by a nasal concha was interesting. May I, through your columns, draw attention to an earlier letter which describes a method to prevent this.[1]

Department of Anaesthesia,
University Hospital and Medical School,
Clifton Boulevard,
Nottingham NG7 2UH
M.J. HARRISON

Reference

1. MACKINNON AG, HARRISON MJ. Nasotracheal intubation—an atraumatic technique. *Anaesthesia* 1979; **34:** 910.

Equipment for paediatric epidurals

There were no paediatric epidural catheters available in Europe until recently and paediatric anaesthetists who wished to perform continuous epidurals in children had to use either paediatric intravenous catheters threaded through 18-gauge Tuohy needles or comparatively large 18-gauge epidural catheters.

Portex has recently perfected a 19-gauge epidural needle with 21-gauge nylon catheter. The needle has a short blunt rounded bevel to prevent injury to the dura, a 5-cm shaft which is graduated every 0.5 cm to allow evaluation of needle progression toward the epidural space, and a cone-shaped catheter introducer inside the needle hub. The catheter has a rounded terminal eye, no lateral holes and is graduated every centimetre to 10 cm with an additional mark at 5 cm and two additional marks at 10 cm. The catheter has a twist on connector.

Six different anaesthetists have put 30 of these catheters into children aged between 3 months and 12 years. They were asked to rate needle, catheter and connector. All found that, after making a hole in the skin, the needle was easy to use because of the graduations and the cone shaped catheter introducer; two found the catheters too long for children under one year (they have since been shortened) and all found the connector easy to use. Catheters were left in place for 24 hours to 8 days and, on examination when removed, nothing abnormal was found at the puncture site or on examination of the catheter itself.

These needles and catheters could be used for children up to 13 years, because the distance from the skin to the epidural space is less than 4 cm.

Departement D'Anesthesie,
Hopital Saint-Vincent De Paul,
74, avenue Denfert-Rochereau,
75674 Paris Cedex 14,
France.

J. DESPARMET

Inhalation of a minitracheotomy tube

We wish to report the inhalation of a minitracheostomy tube, with some suggestions for prevention of this complication.

A 65-year-old man with chronic bronchitis entered the intensive care unit 5 days after oesophagogastrectomy, with sputum retention unresponsive to physiotherapy. On examination, although he was not severely dyspnoeic, he had an increased respiratory rate, 'rattling' breathing and an ineffective cough. A minitracheostomy was performed to prevent further deterioration according to the method described by Matthews and Hopkinson,[1] using the kit produced by Portex U.K. Ltd., (which also incorporates a full instruction sheet). Insertion of the tube proceeded smoothly, apart from some difficulty sliding the tube over the introducer, and it was sutured in place, after distraction of the 'wings' using the Prolene suture provided. Sputum aspiration via the minitracheotomy tube was immediately, and consistently, effective and the patient's respiratory state gradually improved. Nursing staff had occasional difficulty passing a 10FG suction catheter, but were quick to appreciate the advantages of the technique. On the second day, one Prolene suture became loose, and both sutures were replaced by black silk. On the fifth day, the patient started oral fluids, and, during a bout of coughing precipitated by this, inhaled his minitracheotomy tube. A chest radiograph revealed the tube in the right bronchus, whence it was swiftly retrieved by fibreoptic bronchoscopy, under local anaesthesia. The patient suffered no untoward sequelae and was discharged from the unit on the following day. Examination of the tube showed that both sutures were intact.

Whereas faulty suture technique is the obvious avoidable factor in this complication, attention to several points would make its recurrence less likely. Since our sutures were still intact, they must have cut out of the skin. To prevent this, we suggest that prolapse of wings into the stoma should be prevented by ensuring their full distraction prior to suture. Extension of the head is the optimal position for tube insertion, but the head should be at least partially flexed, prior to suture, to reduce skin-stretching, and to allow 'gathering' of loose skin. Prevention of tube prolapse reduces difficulties with suction, with less traction on the sutures. Full thickness bites of skin should be taken when sutures are inserted and two on each side may be advisable. Nursing staff must be aware of the possibility of tube inhalation. Insertion of suction catheters should be as gentle as possible; a smaller catheter should be used if necessary, and the sutures inspected regularly.

Matthews and Hopkinson reported no serious complications in their series of 24 minitracheotomies.[1] The inhalation of the minitracheotomy tube in our patient, although benign, was potentially a serious complication, but we believe that adoption of the simple precautions mentioned above will prevent any recurrence. Our experience of minitracheotomy in this and two other patients to date, convinces us that the technique is a real advance in the management of sputum retention.

Portex UK Ltd., are shortly to market a second version of their minitracheotomy kit, which incorporates changes in design which make inhalation of the tube impossible.

Royal East Sussex Hospital,
Hastings, TN34 1ER.

A.B. LEACH

Reference

1. MATTHEWS HR, HOPKINSON RB. Treatment of sputum retention by minitracheotomy. *British Journal of Surgery* 1984; **71**: 147–50.

EACH "PIECE" PLAYS ITS PART

For an endotracheal tube to work well as a system, each component part should by design and manufacture, be of a high standard.

The wide range of Portex endotracheal tubes are all dedicated to this philosophy and there is a design to suit most needs.

PORTEX

PORTEX LIMITED, Hythe, Kent, England, CT21 6JL.
Tel: Hythe (0303) 66863 & 60551. Telex: 96165. Facsimile: (0303) 66761.

sims A Smiths Industries Medical Systems Company

Association of Anaesthetists of Great Britain and Ireland

APPEAL FOR £600,000

by

31 December 1986

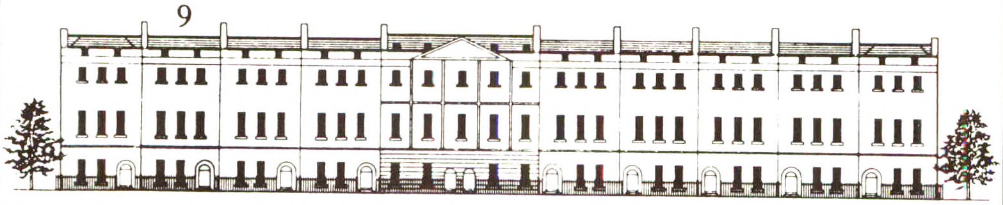
for

REFURBISHMENT and FURNITURE

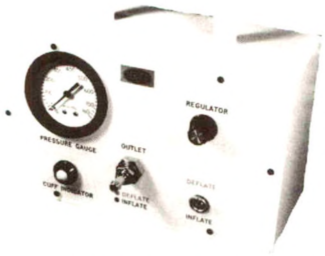
The response has now exceeded £300,000
Visit *your* headquarters to see progress.
Ensure your name is in the book of donors.

Telephone
01–631 1650

9 Bedford Square,
London, WC1B 3RA



AUTOMATIC TOURNIQUET



For ANTIGRAVITY SUIT inflation
ORTHOPAEDIC SURGERY
REGIONAL ANAESTHESIA
– Biert's Block
with comprehensive range of cuffs
and accessories

SCHUCO INTERNATIONAL LONDON LTD
Woodhouse Road, London N12 0NE
Tel: 01 368 1642

NEW from
CDL

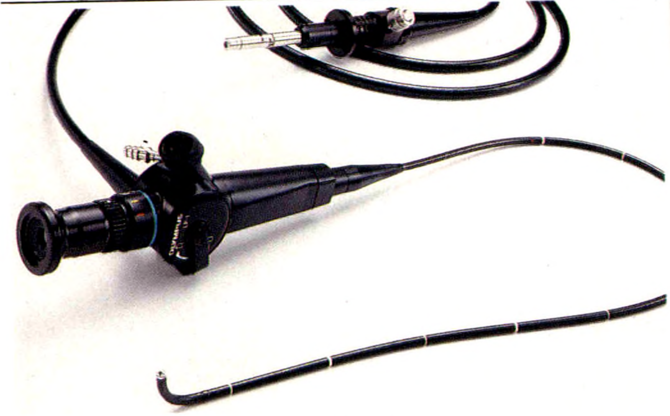
SILICONE RENDELL BAKER
CHILDRENS MASK

The mask for children with minimum dead-space achieved by anatomically correct shape.
Made of soft translucent autoclavable elastomer with 12mm B.S. fitting.
Sizes: 0, 1, 2 & 3

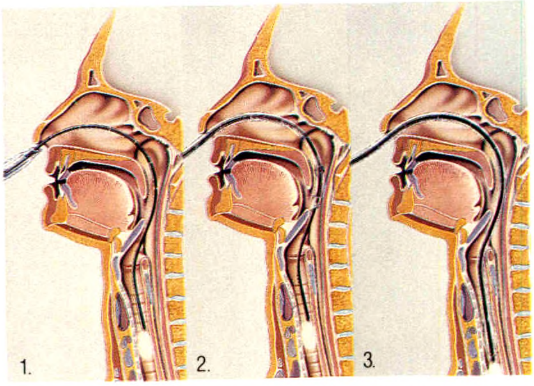
CHILDERHOUSE DEVELOPMENTS LTD
310A Upper Richmond Road West
London SW14 7JN Tel: 01 876 4078

OLYMPUS ENDOSCOPY SYSTEM LF-1 INTUBATING FIBERSCOPE

Specifically designed for anaesthetic use



Fiberoptic bronchoscopes have proved their value for intubating difficult cases*. The LF-1, which is less expensive than current models of bronchoscopes, has been designed to meet the special demands of the procedure. The slimline insertion tube allows a wide range of ET tube diameters to be used, whilst the ergonomic design makes it simple to operate. The LF-1 is an instrument from the OES (Olympus Endoscopy System) range, with the proven benefits of increased durability and immersibility for sterilisation.



1. The LF-1 with the endotracheal tube near the control body, is passed transnasally deep into the trachea.
2. The ET tube is advanced through the nasopharynx using the LF-1 as a 'guide wire'.
3. The ET tube is placed in the trachea, under direct visual control.

---

* 1. Fiberoptic bronchoscopy for anaesthesia. Watson, C.B., Anaesthesiology Review (1982), IX: 17-25.
2. Use of flexible fiberoptic bronchoscope to change endotracheal tubes in critically ill patients. Rosenbaum, S.H., Am. Soc. Anaesthes. (1981), 54: 169-170.
3. Endotracheal intubation with the flexible fiberoptic bronchoscope. Davidson, T.M. Anaesthesiology Review (1975), 54: 346-349.
4. The Broncho-fiberscope as an aid to endotracheal intubation. Taylor, P.A. and Towey R.M. B.J. Anaesth. (1972), 44: 61.

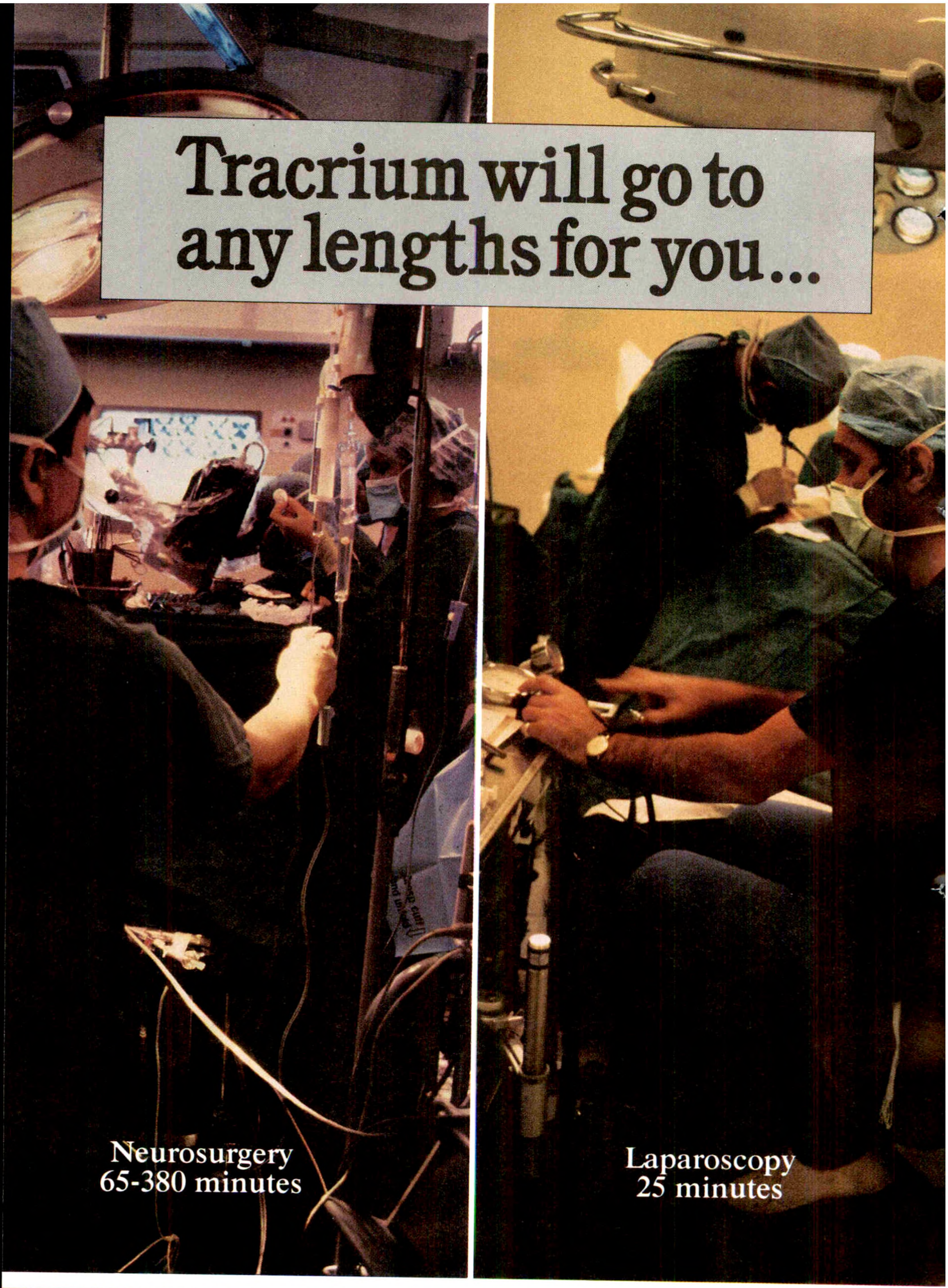
For a demonstration, call Medical Customer Liaison.

OLYMPUS ENDOSCOPY SYSTEM

KeyMed
Specialised Services to Medicine
KeyMed (Medical & Industrial Equipment) Ltd.
KeyMed House, Stock Road, Southend-on-Sea, Essex SS2 5QH.
Telex: 995283, Facsimile: (0702) 65677, Telephone: (0702) 616333 (20 lines).

with subsidiaries:
KeyMed (Ireland) Ltd.
KeyMed House, Lord Edward Court,
Bride Street, Dublin 8.

KeyMed Inc.
400 Airport Executive Park,
Spring Valley, New York, 10977.


Tracrium will go to any lengths for you...
Neurosurgery 65-380 minutes
Laparoscopy 25 minutes

ALMIC MEDICAL
DIVISION
E WELLCOME FOUNDATION LTD

Cardiac valve replacement
103-224 minutes

With Tracrium there are no cumulative effects with supplemental dosing, so the pattern of block and recovery remains consistent, regardless of the number of doses given.

Surgical muscle relaxation can therefore be conveniently extended at a uniform level for as long as required, simply by repeated incremental bolus doses given at predictable clock-timed intervals or by continuous i.v. infusion.

The rate of recovery remains just as rapid as that seen after administration of a single bolus dose, so reversal can be promptly and easily achieved whatever the duration of the operation – regardless of the patient's age and hepatic, renal and circulatory status.

All of which adds up to an unusual degree of versatility.

That's why more and more anaesthetists are using Tracrium routinely, in procedures of widely differing type and length, from laparoscopy to open-heart surgery.

Wellcome

Muscle relaxation without cumulation.

TRACRIUM

Atracurium besylate

(Prescribing information overleaf.)

Tracrium Prescribing Information

Uses Tracrium is a highly selective, competitive (non-depolarising) muscle relaxant for use in a wide range of surgical procedures and to facilitate control of respiration. Tracrium is highly suitable for endotracheal intubation, especially where subsequent relaxation is required.

Dosage and administration

Intravenous injection: Adults and children over 1 year: 0.3-0.6 mg/kg depending on the duration of block required; this will provide relaxation for about 15-35 minutes. Tracrium may be used at standard dosage in elderly patients and in those with respiratory, hepatic or renal failure. Full block can be prolonged with supplementary doses of 0.1-0.2 mg/kg as required. Successive supplementary dosing does not give rise to cumulation. Endotracheal intubation can usually be accomplished within 90 seconds of intravenous injection of 0.5-0.6 mg/kg. The neuromuscular block produced by Tracrium can be rapidly and permanently reversed by standard doses of neostigmine which should be preceded by the administration of atropine. Recovery from full block without the use of neostigmine occurs in about 35 minutes.

Continuous infusion: Tracrium is suitable for administration by continuous infusion at rates of 0.005-0.01 mg/kg/minute (0.3-0.6 mg/kg/hour) to maintain neuromuscular block during long surgical procedures. Tracrium maintains acceptable physical and chemical stability in daylight at concentrations of between 0.5 and 0.9 mg/ml at 30°C for up to: 4 hours in: Compound Sodium Lactate Intravenous Infusion B.P.; 8 hours in: Ringer's Injection U.S.P.; Glucose Intravenous Infusion B.P. 5% w/v; Sodium Chloride 0.18% w/v and Glucose Intravenous Infusion B.P. 4% w/v and up to 24 hours in: Sodium Chloride Intravenous Infusion B.P. Tracrium can be administered by infusion during cardiopulmonary bypass surgery, at the recommended infusion rate. Induced hypothermia to a body temperature of 25 to 26°C reduces the rate of inactivation of atracurium, therefore full neuromuscular block may be maintained by approximately half the original infusion rate at these temperatures.

Contra-indications, warnings, etc. Contra-indicated in patients hypersensitive to atracurium besylate. Tracrium should be used with caution in patients receiving aminoglycosides or polypeptide antibiotics and in patients with myasthenia gravis. In common with all other neuromuscular blocking agents, adequate facilities must be available for endotracheal intubation and artificial ventilation. The neuromuscular block produced by Tracrium may be increased by the concomitant use of inhalational anaesthetics such as halothane. Tracrium should not be mixed in the same syringe with any other agent; in particular it must not be mixed with thiopentone or any alkaline agent, as the high pH would cause inactivation of the Tracrium. As with all other neuromuscular blocking agents the possibility of transient hypotension due to histamine release cannot be excluded. Although animal studies have indicated that Tracrium has no adverse effects on foetal development, nevertheless, like all neuromuscular blocking agents, it should be used with caution in pregnant women. Tracrium may be used to maintain neuromuscular relaxation in Caesarean section as atracurium does not cross the placenta in clinically significant amounts.

Presentation Tracrium injection contains 10 mg per ml atracurium besylate. Two ampoule sizes, 2.5 ml and 5 ml, are available.

Basic NHS costs £6.50 for a box of 5 x 2.5 ml ampoules. £12.50 for a box of 5 x 5 ml ampoules. (PL3/0166).

Further information is available on request.

Calmic Medical Division
The Wellcome Foundation Ltd
Crewe, Cheshire

Wellcome

TRACRIUM

Atracurium besylate

CALMIC MEDICAL DIVISION

ACADEMIC PRESS

publishes books and journals in many areas of Science including:

Acoustics, Agriculture, Anatomy, Anthropology, Archaeology, Audiology

Biochemistry, Biology, Botany

Cancer research, Cardiology, Chemistry, Computer science

Economics, Engineering, Environmental science

Food Science

Geography, Geology

Immunology

Materials technology, Mathematics, Microbiology

Neuroscience, Nutrition

Oncology, Ornithology

Pathology, Pharmacology, Physics, Physiology, Psychiatry, Psychology

Religion

Sociology, Speech, Surgery

Toxicology

Virology

Zoology

BOOKS AND JOURNALS

24-28 Oval Road, London NW1 7DX, U.K.
Orlando, FL 32887, USA.

Anaesthesia, 1986, Volume 41, pages 339–342

Book reviews

Effects of Anesthesia 339
Edited by B.G. Covino, H.A. Fozzard, K. Rehder and G. Strichartz
Handbook of Regional Anaesthesia 339
Edited by P. Prithvi Raj
Mishap or Malpractice 340
C. Hawkins
Anaesthesia. Essays on its History 340
Edited by J. Rupreht, M.J. Lieburg, J.A. Lee and W. Erdmann
Intensive Care Manual 341
Edited by T.E. Oh
Difficulties in tracheal intubation 341
Edited by I.P. Latto and M. Rosen
Searching the Medical Literature 342
J. Welch and T.A. King

Effects of Anesthesia

Edited by B.G. Covino, H.A. Fozzard, K. Rehder and G. Strichartz. Pp. 224, Williams and Wilkins, 1985 £44.

This publication by the American Physiological Society provides, in three sections, series of reviews of the effects of anaesthesia and anaesthetic agents on excitable cell membranes, on the respiratory system and on the cardiovascular system; these are written by experienced researchers in basic science or anaesthesiology departments, with one exception, in the U.S.A. or Canada.

The first section includes chapters on the actions of local or general anaesthetic agents on excitable cell membranes in relation to membrane structure and membrane function. The second section includes chapters on the effects of general anaesthesia on ventilatory control, mechanics of ventilation and in particular, its actions on chest wall function and their significance in relation to pulmonary function during anaesthesia, pulmonary blood flow and pulmonary gas exchange. A final section includes a chapter on the effects of general anaesthesia and specific anaesthetic agents on cardiovascular function dealing particularly with direct and reflex effects and differences between individual volatile anaesthetic agents, followed by chapters on the cardiovascular actions of intravenous anaesthetic agents, narcotic drugs and local anaesthetic agents and regional anaesthetic techniques.

Overall, in addition to providing good general reviews in each of these three areas, the individual sections also provide interesting accounts of fields of current study in a clearly presented, readable and well referenced text. The book is aimed 'at highlighting the intimate relationship and interdependence between anesthesiology and physiology' and is intended for both physiologists and anaesthetists. This book should be of value to anaesthetists in a number of ways, particularly to the clinical anaesthetist, as a useful up-to-date review of some important effects of anaesthesia, and to the trainee anaesthetist studying basic sciences, as a clear account of the significance of anaesthesia in relation to normal physiological function. As such, this book could be recommended to candidates preparing for the Part 2 FFARCS examination.

D. Weatherill

Handbook of Regional Anaesthesia

Edited by P. Prithvi Raj. Pp. 285, Churchill Livingstone, 1985. £44.50.

A number of books have been published in recent years concerning regional blocks. Some are 'how to do it' books and some are more scholarly. This one titles itself a 'Handbook of Regional Anaesthesia' and sets out to fulfil a need occasioned by the current resurgence of interest in regional methods in the USA. It is aimed principally at the American market, though a treatise of this nature is clearly also of interest to British readers. The book itself has a number of unusual characteristics. Of the eighteen contributors, all except one write from the University of Cincinnati, and more than one third have British qualifications. There cannot be many departments of anaesthesia with such a number of members available to contribute ably to a treatise on a sub-specialty interest.

The framework in which the book contents are set out is unusual too. Dr Raj, contributor and editor, starts the volume with a chapter on general principles. The second chapter, entitled 'Rationale and Choice of Regional Anesthesia', discusses the regional techniques applicable in neurosurgery, ophthalmic, ear nose and throat, urology, renal transplant, orthopaedics, general and vascular surgery. Each sub-section has its own authorship. There are then individual chapters on obstetrics, postoperative pain and chronic pain. Only now does the reader come upon the sixth chapter, on the physiology, pharmacology and toxicity of local anaesthetics. Chapter 7 then describes the techniques of nerve blocking not already considered in the early chapters. Finally, there are chapters on adjuvant techniques and complications. The unusual arrangement of chapters and the multiplicity of authors may at first confuse the reader. For example, spinal blockade and epidural block, being applicable to a wide range of surgical operations, receive a short discussion in a number of sections as well as the main treatment in the chapter on techniques of nerve blocking. There is, therefore, a degree of repetition, though this is not necessarily a bad thing. Some of the statements are rather synoptic in nature, little more in fact than a sentence with a reference. Many readers would welcome elaboration with an indication of the practical importance of statements made. The overall text would be improved if cross-references were employed to help the reader.

The British reader will note that the text has been written with the American practitioner principally in mind. This is not a disadvantage, since the few changes in usage of drug names should be understood in Britain without difficulty. The clinical practice is not significantly different between Britain and the USA. Nevertheless, most of the references quoted are to the North American literature and the reader will search in vain for mention of some developments in the UK. Among the most important of these is the abandonment of bupivacaine in Britain for intravenous regional analgesia, due to the reports of intractable myocardial depression; the drug is still advocated for this purpose in this volume.

The illustrations in the volume are good. The line drawings are without exception clear, with a lack of unnecessary material, and they all make their point. The index is not entirely satisfactory. In an effort to be exhaustive there are nearly two complete pages of entries under the heading 'Anesthesia'. Surely this results in unnecessary duplication.

Your reviewer has made a number of criticisms, but it must be emphasised that there is a lot of information provided in this Handbook. Not only will the practitioner of regional block find helpful 'how to do it' sections, but he will also obtain background theoretical information and, where this needs to be amplified, the reference sources are quoted. This book can be recommended to British anaesthetists, albeit with some reservations.

R.S. Atkinson

Mishap or Malpractice

By C. Hawkins. Pp. 316, Blackwells, 1985. £8.50.

This book, written by a physician who claims no special medicolegal prowess, is published to mark the centenary of the Medical Defence Union. Not surprisingly, therefore, large parts of it bear considerable similarity to the horror stories usually contained in any of the defence organisations' annual reports. But there is more to *Mishap or Malpractice* than that. It contains a considerable amount of the fascinating history of defence systems for doctors from 1885 to the present. The author also deals with the current position and describes the attitudes of the public, the law and the practitioners of medicine. Many famous cases are outlined as examples, and thus the book will be a source of reference to medicolegal cases for the non-lawyer. It also presents, in a modestly balanced manner, many of the subjects of medicolegal interest but there is neither interpretation of the present nor much speculation about the future.

Every chapter is headed by a quotation; for example, chapter 3, 'The MDU is a shield but the arbiter is the law'—but should there be a shield for an anaesthetist who does not visit his patients, who in the course of an extensive surgical procedure does not take or make a record of the blood pressure, or is unaware that his patient was grossly incapacitated within 6 hours of general surgery? These may be matters of debate within our specialty but what is, in the reviewer's opinion, quite clear is that the patient's estate should not be decimated in the attempt by relatives to obtain financial support for a crippled individual. This matter is mentioned briefly in the context of no fault compensation.

It is not a book for the narrow specialist; it is for all doctors to read and to apply in their own discipline, and it should be available in all medical libraries.

J.N. Lunn

Anaesthesia. Essays on its History

Edited by J. Rupreht, M.J.V. Lieburg, J.A. Lee and W. Erdmann. Pp. 409, Springer-Verlag, 1985. DM 118.

This book is, in reality, the Proceedings of the First International Symposium on the History of Modern Anaesthesia, held in Rotterdam in 1982. The essays are therefore based on the lectures given at that time and have been divided into five main sections for this edition. These sections are: pioneers in anaesthesia (including amongst others Clover, Magill, Waters and Lundy), development of techniques (including amongst others intravenous anaesthesia, dissociative anaesthesia, cardiothoracic anaesthesia, neurosurgical anaesthesia and closed circuit anaesthesia), regional developments in anaesthesia (outlining how anaesthesia spread throughout the world, country to country), the World organisation (development of the World

Federation and various societies) and humanism in anaesthesia (anything which did not fit in the other sections!). This is not a fully comprehensive book. There are many great pioneers ignored, techniques that are not described and several countries remain unmentioned.

The Rotterdam Meeting attracted a large number of the great names of anaesthesia, together with often younger anaesthetic historians. This is reflected in the book. The younger age group have presented carefully researched history, while those in the older age groups produced personal reminiscences of their own contributions to the specialty. Both are equally valuable, but the personal reflections are particularly interesting and permit unique insights into certain developments.

It is particularly welcome to see so many historical papers from places other than England and America available in English. Much of the geographical spread of anaesthesia has been unknown, except within individual countries, and this volume provides much information for the interested reader and does much to encourage a more global appreciation of anaesthetic history.

Lectures are usually accompanied by visual aids, either models, actual equipment, slides or films, which enhance the speaker's ideas. Proceedings tend to omit these important adjuncts and this volume is unfortunately no exception. Only nine out of eighty-three essays include significant numbers of photographs or diagrams—a sad omission.

Each essay is relatively short, only four to five pages on average, which makes it easy to dip into and then leave again to return later. There are particularly valuable reference sections after each presentation and a comprehensive index permits a rapid scanning process for those searching for a particular name or detail. Many fascinating historical facts became apparent during the question times permitted after each paper in Rotterdam; these details have unfortunately not been included and are thus presumably lost.

Despite the minor drawbacks outlined above, this slim volume provides a great wealth of historical facts and opinions, collated from the Rotterdam Symposium, which have been previously unavailable. It will be essential reading for all those with an interest in anaesthetic history, but some may be deterred by its relatively high price.

It is to be hoped that a further volume of essays in what may become a series will follow the Second International Congress on the History of Anaesthesia which is to be held in London in 1987, and may well fill some of the gaps left by this book.

D.J. Wilkinson

Intensive Care Manual

Edited by T.E. Oh. Pp. 463, The Butterworth Group, 1985. £25.00.

The second edition of this manual has recently been published and is aimed, very much like the first edition, towards both senior and junior medical staff working in a general intensive care unit. It is also intended for use by nursing staff working in these units, and doctors working in peripheral areas who may occasionally have to manage critically ill patients. The book has been designed to provide useful practical information which is readily available and is not meant as a reference work giving very detailed information on any specific subject.

There are now 33 contributors drawn from several centres in Australia, most of whom are working full time in intensive care. New sections have been included on 'Obstetrical Emergencies' and 'Paediatric Intensive Care', which are intended for use by those confronted with such problems at infrequent intervals. A further short section on 'Infections' has been included, together with updating of the other sections to include some new chapters, recent advances and further references. The book is divided into sections covering body systems and then further sections covering such subjects as shock, physical injuries, poisoning, metabolic and haematological aspects, pain relief and monitoring.

With many authors it is inevitable that there are changes in style between individual chapters. Some chapters give a very concise summary of the subject matter, which may include lists or tables, whereas others cover the subject in a style more related to the traditional textbook. In one or two instances, I would have wished for a little more information, for instance in the use of intravenous narcotics.

In a typical chapter, established principles and methods of treatment are presented together with brief discussion of less well accepted methods. Inevitably, there are developments in some fields following the writing of any textbook, however this book succeeds in giving at least a brief mention of some recently introduced drugs and of possible future changes in methods of treatment. Each chapter is followed by a list of references as an aid to further reading, and there are appendices which cover normal biochemical values, SI units, symbols and values in respiratory physiology, physiological equations, plasma drug concentrations and American nomenclature. All of these form a most useful rapid reference section.

The overall impression is that the manual is very well suited to its intended readership, gives wide coverage of the subject in a concise format and is a most useful volume to have at one's side in the intensive care unit.

D.H. Short

Difficulties in tracheal intubation

Edited by I.P. Latto and M. Rosen. Pp. 183, Baillière Tindall, 1985. £14.50.

This excellent book brings together information which hitherto has been available, although scattered in the literature. There are contributions from six authors, all anaesthetists, providing a comprehensive survey of all matters relating to intubation of the trachea. Some slight repetition between chapters is therefore almost inevitable, but where key issues are concerned, this is probably no bad thing.

There is a logical sequence of chapters dealing with anatomy, both adult and paediatric, pathophysiology of complications, the cuff, techniques of awake intubation. A series of well chosen case reports makes compulsive and memorable reading, forcing the reader to come to grips with the reality of the subject. A chapter on obstetric anaesthesia is short by comparison, yet the facts are presented in a didactic manner which is probably all important in the initial training of anaesthetists. Bronchial intubation is also thoroughly covered and a final chapter is imaginatively devoted to the teaching of intubation.

Concisely and lucidly written, the book is eminently readable. It will serve as a useful reference for the experienced anaesthetist who, sooner or later, will be faced with a problem intubation, as well as for the tiro who will find all the information he may seek on the subject. It is lavishly illustrated and amply referenced, well printed and bound. It can be unreservedly recommended for anyone with an interest in the subject. It is a must for any anaesthetic department and the individual who buys his own copy will not regret it.

I.D. LEVACK
A.H.B. MASSON

Searching the Medical Literature

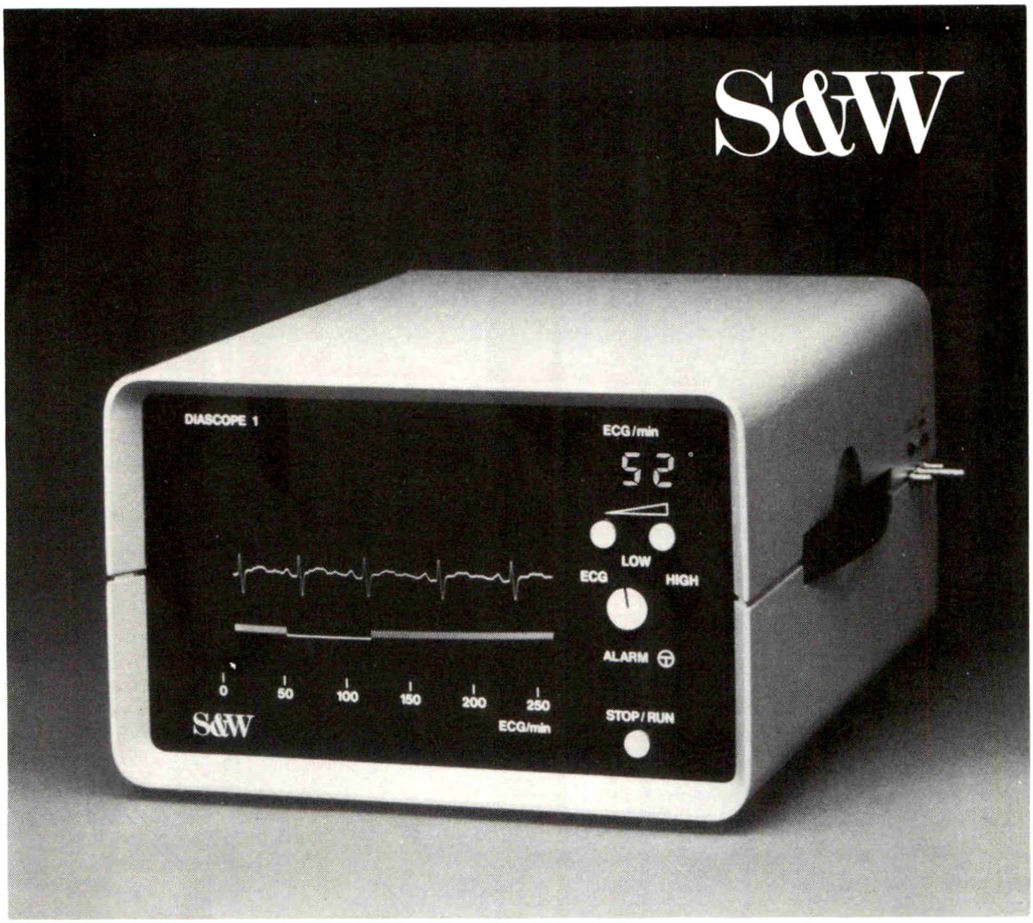
By J. WELCH AND T.A. KING. Pp. 154, Chapman and Hall Ltd., 1985. £15.00.

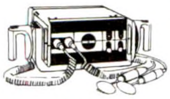
This book, written jointly by an information officer and a librarian for all medical and paramedical personnel, describes printed and computer-based guides to the primary medical literature of periodicals, books and reports. It is not specifically directed at anaesthetists, but the selection of sources described suggests that clinicians generally are envisaged as the major target audience.

An introductory chapter glancing at recent developments in medical information services is followed by two chapters describing a range of printed and online tools for searching the periodical literature. Succeeding chapters are devoted to: drug information services (a useful account written by a pharmacist), sources of statistical information, the scope and contents of a reference collection, a slightly confusing section on background reading and, finally, a guide to sources of advice for doctors as authors, speakers or committee members. Some of the lists of recommended reading might have tempted the interested reader more by offering a less niggardly selection.

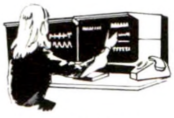
Perhaps not many doctors will read this book from cover to cover, but many would benefit from a selective reading. As well as discovering or rediscovering various ways of exploiting the medical literature, readers may also be encouraged to look afresh at the services and resources offered by their local medical library. Knowledgeable and demanding users are welcome and powerful allies for librarians seeking to improve the levels of library provision in the NHS.

S. PRITCHARD

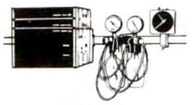




Defi 2
multipurpose defibrillator

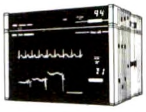


Central Station
up to 12 patients monitored and recorded.

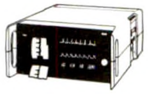


Modura Rail
The original "Danish Rail" system

Medicart
Multipurpose trolleys designed especially for medical use.



8000 series
– the complete flexible monitoring system



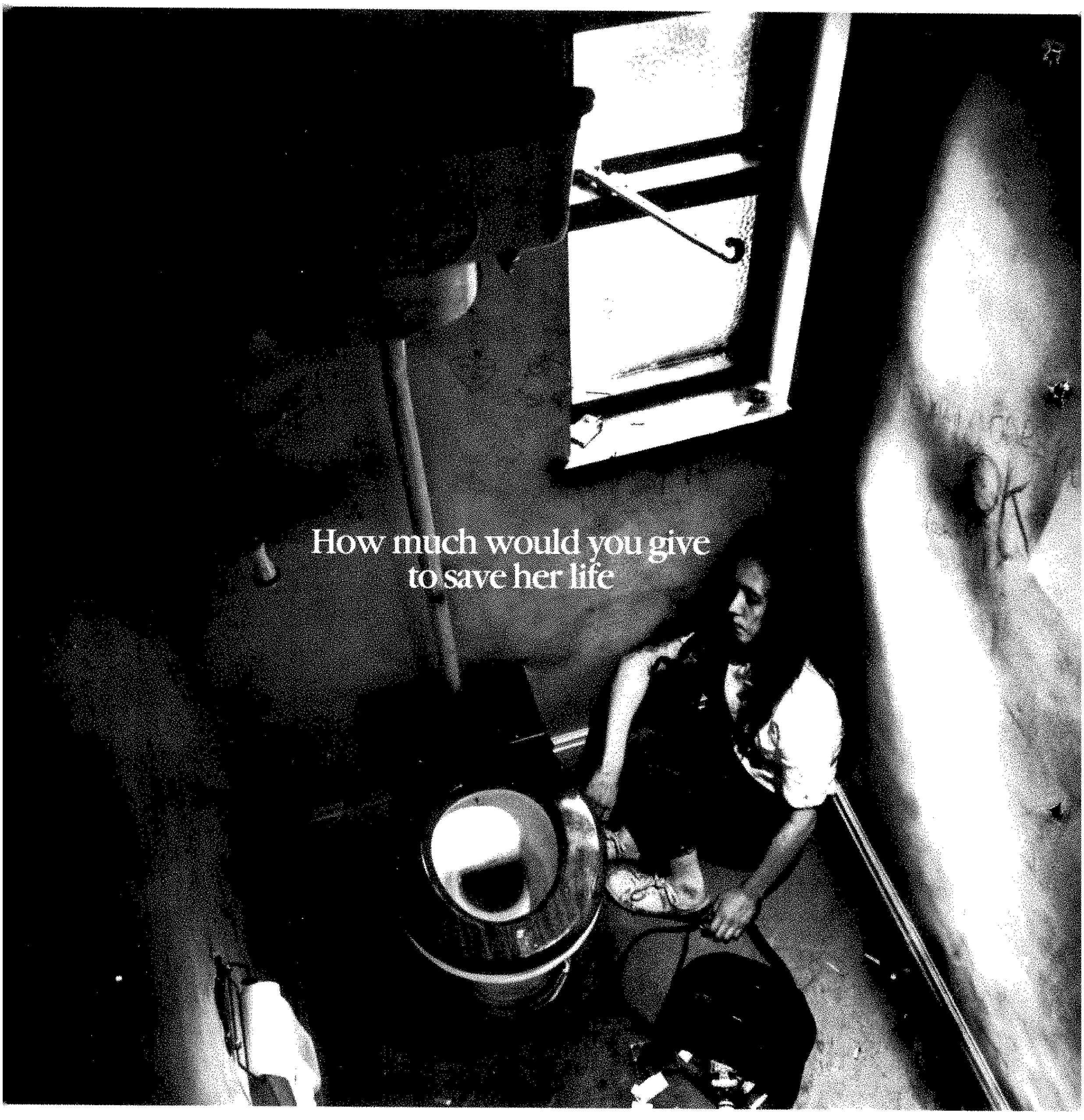
Diascope 2
twin channel monitor in 16 configurations

Simonsen & Weel ... care

The popular Diascope 1 has now been upgraded to include integral rate alarms, pacemaker discriminator and full micro-processor support of controls, whilst retaining the proven performance of its popular predecessor. The latest improvements mean that more than ever the Diascope 1 is the ideal monitor for use throughout the hospital.
Equally suited to stand alone use in the neonatal unit, operating theatre or general ward situation through to use in the ICU/CCU linked to the compatible 8600 Central Station.
Improvements that show once again, Simonsen and Weel . . . care.

Simonsen & Weel Ltd. Ruxley Corner, Sidcup, Kent DA14 5BL Tel: 01-309 0433 Telex: 896328

[illegible] solution contains 0.4mg naloxone hydrochloride. Narcan* Neonatal (2ml ampoules) – each 1ml of solutic contains 0.02mg naloxone hydrochloride. **Uses**: Diagnosis and reversal of respiratory and other CNS effects of opioids, including those in the newborn following opioid administration to the mothe **Dosage and Administration**. **Adults**: For opioid overdose give 0.4mg to 2mg intravenously. Repeat at 2 to 3 minute intervals if required. For post-operative use give 0.1-0.2mg intravenously allowing minutes between each 0.25ml (0.1mg) increment. In certain circumstances (eg. overdosage of long-acting opioid) give intravenous infusion. Dilute in 0.9% saline or 5% dextrose in water or saline (2mg i Narcan in 500ml = 0.004mg/ml). Use infusion mixtures within 24 hours. Titrate infusion according to response. **Children**. For opioid overdose, initially 0.01mg (10 micrograms) per kg intravenous, repeating with 0.1mg (100 micrograms) per kg if response unsatisfactory. **Neonates**. Establish adequate airway first. Usually 0.01mg/kg i.v., i.m. or s.c. for opioid-induced depression, repeated as for adu guidelines. Alternatively give a single intramuscular dose of 200 micrograms at birth. **Contra-Indications**. Hypersensitivity to Narcan. **Precautions, Warnings**: A withdrawal syndrome may occur in opioi dependent patients, neonates delivered of such patients, and chronic opioid users. Usual precautions in pregnancy. Keep patients under observation as Narcan has a short duration of action and repe doses may be necessary. Care in patients with compromised cardiac function as there are two reports of ventricular tachycardia and fibrillation. **Adverse Effects**. Occasionally, nausea and vomitin especially when larger than recommended doses used. **Product Licence Nos**. Narcan – Ampoule 4524/0001 Narcan – Vial 4524/0001 Narcan Neonatal 4524/0002. **NHS Price**: Narcan – Ampoule (bo of 10 x 1ml amps) £46.21. Narcan – Vial (1 x 10ml vial) £41.59. Narcan Neonatal (box of 10 x 2ml amps) £33.54. Further information is available on request from the company. Du Pont (UK) Limite Pharmaceuticals, Wedgwood Way, Stevenage, Hertfordshire SG1 4QN. Telephone: (0438) 734549. *Narcan is a registered trademark of E.I. Du Pont de Nemours & Co. Inc.


How much would you give
to save her life

For a known or suspected opioid overdose, the initial adult dose of Narcan* is 0.4-2.0mg i.v. repeated, if necessary, up to 10mg.

These larger doses of Narcan may be necessary to diagnose the presence of opioids such as dextropropoxyphene, whose respiratory depressant effects in overdose are particularly hard to reverse.

Overdoses caused by long-acting opioids, such as methadone, may necessitate repeated administration of Narcan to prevent recurrent narcosis.

In both these situations, the new Narcan 10ml vial offers a convenient alternative to existing 1ml ampoules. The 10ml vial also greatly simplifies the administration of Narcan by infusion.

NARCAN*
(naloxone hydrochloride)

New 10ml vial

Same strength,
larger volume

Du Pont Pharmaceuticals

Anaesthesia, 1986, Volume 41, pages 343–349

Anaesthetic literature

This section of *Anaesthetic literature contains references taken from Current Contents—Life Sciences* for September 1985. The journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennysylvania, USA.

Abdominal surgery

Volume-controlled high frequency positive pressure ventilation for upper abdominal surgery. A clinical report. BABINSKI, M.F., SMITH, R.B., SJOSTRAND U. *Anaesthesia* 1985; **40:** 619.

Effects of morphine and atropine on motility and transit in the human ileum. BORODY, T.J., QUIGLEY, E.M.M. *et al. Gastroenterology* 1985; **89:** 562.

Characterization of segmental collateral blood flow in the small intestine. BULKLEY, G.B., WOMACK, W.A. *et al. American Journal of Physiology* 1985; **249:** G228.

Opioid inhibition of synaptic transmission in the guinea-pig myenteric plexus. CHERUBINI, E., MORITA, K., NORTH, R.A. *British Journal of Pharmacology* 1985; **85:** 805.

Effect of nicotine on blood flow, oxygen consumption and glucose uptake in the canine small intestine. GRAYSON, J., OYEBOLA, D.D.O. *British Journal of Pharmacology* 1985; **85:** 797.

Laser-doppler, H_2 clearance, and microsphere estimates of mucosal blood flow. KVIETYS, P.R., SHEPHERD, A.P., GRANGER, D.N. *American Journal of Physiology* 1985; **249:** G221.

Regional blood flow and water content of the obstructed small intestine. PAPANICOLAOU, G., NIKAS, D. *et al. Archives of Surgery* 1985; **120:** 926.

Colonic anastomotic healing and oxygen tension. SHANDALL, A., LOWNDES, R., YOUNG, H.L. *British Journal of Surgery* 1985; **72:** 606.

Pharmacology

Adrenergic drugs and their antagonists

Inhibition of human neuroblastoma by dopamine antagonists. MCGRATH, P.C., NEIFELD, J.P. *Surgery* 1985; **98:** 135.

Clinical pharmacological studies on the interaction between alpha-adrenoceptors and calcium antagonists. REID, L.J., PASANISI, F. *et al. Journal of Cardiovascular Pharmacology* 1985; **7:** S206 (Suppl).

Does dopamine suppress stress-induced intestinal and renal vasoconstriction? WINSO, O., BIBER, B., MARTNER, J. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 508.

Anaesthetic agents

Probenecid impairment of acetaminophen and lorazepam clearance—direct inhibition of ether glucuronide formation. ABERNETHY, D.R., GREENBLATT, D.J. *et al. Journal of Pharmacology and Experimental Therapeutics* 1985; **234:** 345.

Althesin in high risk patients with heart disease in orthopedic surgery. BARBERO, C., BIOLINO, P. *et al. International Journal Clinical Pharmacology Therapy and Toxicology* 1985; **23:** 384.

Effects of anaesthetics on protein synthesis in isolated rat hepatocytes. BESSESEN, A., MORLAND, J. *Acta Pharmacologica et Toxicologica* 1985; **57:** 23.

Effects of etomidate on cortisol biosynthesis in isolated guinea-pig adrenal cells: comparison with metyrapone. DE COSTER, R., BEERENS, D. *et al. Journal of Endocrinological Investigation* 1985; **8:** 199.

The effect of cimetidine on the formation of methoxyflurane fluorometabolites in mice. FRY, B.W., CIARLONE, A.E., COALSON, B.E. *Research Communications in Chemical Pathology and Pharmacology* 1985; **49:** 163.

Chemistry of halothane–enflurane mixtures applied to anesthesia. KORMAN, B., RITCHIE, I.M. *Anesthesiology* 1985; **63:** 152.

Isoflurane (leading article). *Lancet* 1985; **2:** 537.

The effect of diazepam on genioglossal muscle activity in normal human subjects. LEITER, J.C., KNUTH, S.L. *et al. American Review of Respiratory Disease* 1985; **132:** 216.

Analysis of respiratory patterns in the awake and in the halothane anaesthetised rat. MARTIN-BODY, R.L.,

---

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London, WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. An exact copy of the monthly section or various cumulative classifications of the Anaesthetic Literature published in the Journal can be obtained on application to him. References from January 1984 have been entered on data base and search facilities are also available. All communications about this matter should be addressed to Dr Kaufman please.

SINCLAIR, J.D. *Respiration Physiology* 1985; **61:** 105.

Etomidate anesthesia inhibits the cortisol response to surgical stress. MEHTA, M.P., DILLMAN, J.B. *et al. Acta Anaesthesiologica Scandinavica* 1985; **29:** 486.

Possible mechanisms of action of diazepam as an adenosine potentiator. MORITOKI, H., FUKUDA, H. *et al. European Journal of Pharmacology* 1985; **113:** 89.

Oxygen—friend and foe. NUNN, J.F. *Journal of the Royal Society of Medicine* 1985; **78:** 618.

Influence of injectable anaesthetic combinations on blood gas tensions and acid-base status in laboratory rats. SVENDSEN, P., CARTER, A.M. *Acta Pharmacologica et Toxicologica* 1985; **57:** 1.

Responsiveness to oral diazepam in the elderly: relationship to total and free plasma concentrations. SWIFT, C.G., EWEN, J.M. *et al. British Journal of Clinical Pharmacology* 1985; **20:** 111.

Effects of halothane on the development of rat brain: a golgi study of dendritic growth. UEMURA, E., IRELAND, W.P. *et al. Experimental Neurology* 1985; **89:** 503.

Etomidate infusion and adrenocortical function. A study in elective surgery. WANSCHER, M., TONNESEN, E. *et al. Acta Anaesthesiologica Scandinavica* 1985; **29:** 483.

Comparative actions of pentobarbital and verapamil on canine cerebral and peripheral arteries. WENDLING, W.W., HARAKAL, C. *Research Communications in Chemical Pathology and Pharmacology* 1985; **49:** 189.

Effect of general anaesthetics and organic solvents on alpha 1-adrenoceptors in the myometrium. WIKBERG, J.E.S., HEDE, A.R., LINDAHL, M. *Acta Pharmacologica et Toxicologica* 1985; **57:** 53.

Analgesic agents

Influence of morphine on the distal oesophagus and the lower oesophageal sphincter—a manometric study. DOWLATSHAHI, K., EVANDER, A. *et al. Gut* 1985; **26:** 802.

Opioid effects on lidocaine disposition and toxicity in mice. GARTY, M., BENZVI, Z., HURWITZ, A. *Journal of Pharmacology and Experimental Therapeutics* 1985; **234:** 391.

Interactions of codeine-7, 8-oxide (codeine-epoxide), as a new metabolite of codeine, with multiple opiate receptors. KONNO, F., SATO, Y. *et al. General Pharmacology* 1985; **16:** 379.

Differential effects of morphine on core temperature in stressed and non-stressed rats. USHIJIMA, I., TANAKA, M. *et al. European Journal of Pharmacology* 1985; **112:** 331.

Other drugs

Minireview. Ethanol, the choline requirement, methylation and liver injury. BARAK, A.J., TUMA, D.J., BECKENHAUER, H.C. *Life Sciences* 1985; **37:** 789.

Rifampicin reduces bioavailability of chloramphenicol and verapamil. D'ARCY, P.F. *Pharmacy International* 1985; **6:** 149.

The molecular pharmacology and structural features of calcium channels. FERRY, D.R., GOLL, A. *et al. British Journal of Clinical Pharmacology* 1985; **20:** 233S (Suppl 2).

The pharmacology of spasticity. LENMAN, J.A.R. *Recent Achievements in Restorative Neurology*, Eds Eccles, J., Dimitrijevic, M.R., 1985; **1:** 31.

Clinical pharmacokinetics of ergotamine in migraine and cluster headache. PERRIN, V.L. *Clinical Pharmacokinetics* 1985; **10:** 334.

The effect of ranitidine on the disposition of lignocaine. ROBSON, R.A., WING, L.M.H. *et al. British Journal of Clinical Pharmacology* 1985; **20:** 170.

Apparatus

The effect of a gas leak around the endotracheal tube on the mean tracheal pressure during mechanical ventilation. FONTAN, J.J.P., HELDT, G.P., GREGORY, G.A. *American Review of Respiratory Disease* 1985; **132:** 339.

The cult of the swan-ganz catheter: overuse and abuse of pulmonary flow catheters. ROBIN, E.D. *Annals of Internal Medicine* 1985; **103:** 445.

Estimation of ventilation-perfusion inequality by inert gas elimination without arterial sampling. WAGNER, P.D., SMITH, C.M. *et al. Journal of Applied Physiology* 1985; **59:** 376.

Complications

Myasthenic crisis after intravenous administration of iodinated contrast agent. CHAGNAC, Y., HADANI, M., GOLDHAMMER, Y. *Neurology* 1985; **35:** 1219.

A nasty shock from antibiotics? Editorial. *Lancet* 1985; **2:** 594.

Magnesium toxicity as a cause of hypotension and hypoventilation. FASSLER, C.A., RODRIGUEZ, M. *et al. Archives of Internal Medicine* 1985; **145:** 1604.

Aspiration in head and neck surgical patients. LOGEMANN, J.A. *Annals of Otology, Rhinology and Laryngology* 1985; **94:** 373.

HLA antigens in patients with unexplained hepatitis following anesthesia. OTSUKA, S., YAMAMOTO, M. *et al. Acta Anaesthesiologica Scandinavica* 1985; **29:** 497.

General anaesthetic procedures

Anaesthesia for minor procedures in children with malignant disease. HAIN, W.R., TOMLINSON, J.H., BARBOR, P.R.H. *Journal of the Royal Society of Medicine* 1985; **78:** 715.

Anesthetic management in patients with pheochromocytoma. Hauss, G.-M., Van Aken, H., Lawin, P. *Cardiology* 1985; **72:** 174.

General interest

Vertebrobasilar insufficiency: a review. Ausman, J.I., Shrontz, C.E. *et al. Archives of Neurology* 1985; **42:** 803.

Laboratory tests and diagnostic procedures in evaluation of liver disease. Chopra, S., Griffin, P.H. *American Journal of Medicine* 1985; **79:** 221.

Diagnosis and management of pheochromocytoma. Gifford, R.W., Bravo, E.L., Manger, W.M. *Cardiology* 1985; **72:** 126.

Molecular genetics of acute intermittent porphyria. Goldberg Sir A. *British Medical Journal* 1985; **291:** 499.

Clinical and biochemical aspects of pheochromocytoma. Report of 110 cases. Januzzewicz, W., Wocial, B. *Cardiology* 1985; **72:** 131.

Myotonic muscular dystrophy. Roses, A.D. *Archives of Internal Medicine* 1985; **145:** 1487.

Undiagnosed phaeochromocytoma in the perioperative period. Case report. Sellevold, O.F., Raeder, J., Stenseth, R. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 474.

I-MIBG—a new agent in diagnosis and treatment of pheochromocytoma. Shapiro, B., Sisson, J.C. *et al. Cardiology* 1985; **72:** 137.

Myotonic dystrophy. Tanaka, K. *Medical Hypotheses* 1985; **17:** 415.

Local analgesia

Pharmacokinetics of lignocaine in humans after perioral injections. Gadalla, M.A.F., Sabri, S. *Drug Development and Industrial Pharmacy* 1985; **11:** 1597.

Spinal opioids

Epidural sufentanil for postoperative pain relief. Donadoni, R., Rolly, G. *et al. Anaesthesia* 1985; **40:** 634.

Minireview. Peptidases that terminate the action of enkephalins. Dua, A.K., Pinsky, C., Labella, F.S. *Life Sciences* 1985; **37:** 985.

Interaction of dynorphin with kappa opioid receptors in bovine adrenal medulla. Dumont, M., Lemaire, S. *Neuropeptides* **6:** 321.

Diuresis and suppression of vasopressin by kappa-opioids—comparison with mu-opioids and delta-opioids and delta-opiods and clonidine. Leander, J.D., Zerbe, R.L., Hart, J.C. *Journal of Pharmacology and Experimental Therapeutics* 1985; **234:** 463.

Use of intrathecal morphine for postoperative pain relief relief following lumbar spine surgery. O'Neill, P., Knickenberg, C. *et al. Journal of Neurosurgery* 1985; **63:** 413.

Epidural morphine prophylaxis of postoperative pain. Report of a double-blind multicentre study. Writer, W.D.R., Hurtig, J.B. *et al. Canadian Anaesthetists' Society Journal* 1985; **32:** 330.

Obstetric anaesthesia and analgesia

Current concepts: the management of thyrotoxicosis in pregnancy. Burrow, G.N. *New England Journal of Medicine* 1985; **313:** 562.

Effects of intravenous ritodrine on lactate and pyruvate levels—role of glycemia and anaerobiosis. Cano, A., Martinez, P. *et al. Obstetrics and Gynecology* 1985; **66:** 207.

Effects of anesthesia for repeat cesarean section on postoperative infectious morbidity. Chestnut, D.H. *Obstetrics and Gynecology* 1985; **66:** 199.

Maternal heart rate in pregnancy. Clapp, J.F. *American Journal of Obstetrics and Gynecology* 1985; **152:** 659.

Antihypertensive treatment in pregnancy: analysis of different responses to oxprenolol and methyldopa. Gallery, E.D.M., Ross, M.R., Gyory, A.Z. *British Medical Journal* 1985; **563:** 14.

Behavioral states in the human fetus during labor. Griffin, R.L., Caron, F.J.M., Van Geijn, H.P. *American Journal of Obstetrics and Gynecology* 1985; **152:** 828.

Association of elective repeat cesarean delivery and persistent pulmonary hypertension of the newborn. Heritage, C.K., Cunningham, M.D. *American Journal of Obstetrics and Gynecology* 1985; **152:** 627.

Current concepts: hypertension in pregnancy. Lindheimer, M.D., Katz, A.I. *New England Journal of Medicine* 1985; **313:** 675.

Fatal pulmonary oedema associated with the use of ritrodrine in pregnancy. Case report. MacLennan, F.M., Thomson, M.A.R. *et al. British Journal of Obstetrics and Gynaecology* 1985; **92:** 702.

Vasopressin reduces blood loss from second-trimester dilatation and evacuation abortion. Schulz, K.F., Grimes, D.A., Christensen, D.D. *Lancet* 1985; **2:** 353.

Pregnancy: increased effect of verapamil in human uterine arteries. Spanish, M.S., Nelson, S.H. *et al. European Journal of Pharmacology* 1985; **112:** 387.

Catecholamines in amniotic fluid as indicators of intrapartum fetal stress. Yashiro, Y., Kudo, T., Kishimoto, Y. *Acta Medica Okayama* 1985; **39:** 253.

Paediatric anaesthesia and intensive care

Hemodynamic and acid-base effects of promazine on unanaesthetized pregnant sheep and fetus. Ayromlooi, J. *Developmental Pharmacology and Therapeutics* 1985; **8:** 302.

Prevention of intraventricular haemorrhage by fresh frozen plasma. Beverley, Pitts-Tucker *et al. Archives of Disease in Childhood* 1985; **60:** 710.

Ventilation, hyperventilation, megaventilation, and cerebral blood flow. Bruce, D.A. *Brain Insults in Infants and Children: Pathophysiology and Management*. Ed. James, H.E. *et al.* 1985; 257.

Influence of 2,3-diphosphoglycerate (DPG) concentration in maternal red cells on the transplacental exchange of respiratory gases. Carter, A.M., Gronlund, J. *Physiological Development of the Fetus and Newborn*. Ed. Jones, C.T., Nathanielsz, P.W. 1985; 47.

Prevention of neonatal respiratory distress syndrome by tracheal instillation of surfactant—a randomized clinical trail. Enhorning, G., Shennan, A. *et al. Pediatrics* 1985; **76:** 145.

Near-miss sudden infant death syndrome in 8 infants with sleep apnea-related cardiac arrhythmias. Guilleminault, C., Ariagno, R. *et al. Pediatrics* 1985; **76:** 236.

Influence of vagal activity on the neonatal ventilatory response to hypoxemia. Laframboise, W.A., Woodrum, D.E., Guthrie, R. *Pediatric Research* 1985; **19:** 903.

Changes in plasma arginine vasopressin during transition from fetus to newborn following minimal trauma delivery of lambs and goats. Leffler, C.W., Crofton, J. *et al. Biology of the Neonate* 1985; **48:** 43.

Risk factors for neonatal hyperglycemia associated with 10% dextrose infusion. Louik, C., Mitchell, A.A. *et al. American Journal of Diseases of Children* 1985; **139:** 783.

Management of the child in shock. Perkin, R.M. *Brain Insults in Infants and Children: Pathophysiology and Management*. Ed. James, H.E. *et al.* 1985; 201.

Control of fluid and electrolyte balance during fetal life. Robillard, J.E., Nakamura, K.T., Ayres, N.A. *Physiological Development of the Fetus and Newborn*. Ed. Jones, C.T. and Nathanielsz, P.W. 1985; 527.

Placental transfer of lidocaine and elimination from newborns following obstetrical epidural and pudendal anesthesia. Sakuma, S., Tka, T. *et al. Pediatric Pharmacology* 1985; **5:** 107.

Prolonged expiratory apnoea: a disorder resulting in episodes of severe arterial hypoxaemia in infants and young children. Southall, D.P., Talbert, D.G. *et al. Lancet* 1985; **2:** 571.

Cardiovascular system

Physiology

Myocardial metabolic and morphometric changes during canine endotoxin shock before and after glucose–insulin–potassium. Bronsveld, W., Van-Lambalgen, A.A. *et al. Cardiovascular Research* 1985; **19:** 455.

Control of gastric vascular resistance in cardiogenic shock. Bulkley, G.B., Oshima, A. *et al. Surgery* 1985; **98:** 213.

Cardiac mechanics and energetics: chemomechanical transduction in cardiac muscle. Gibbs, C.L., Chapman, J.B. *American Journal of Physiology* 1985; **249:** H199.

Increased numbers and stimulation of migration, phagocytosis and chemiluminescence following abdominal surgery. Neoptolemos, J.P., Wood, P. *et al. European Surgical Research* 1985; **17:** 215.

Bradycardia during reversible haemorrhagic shock—a forgotten observation? Secher, N.H., Bie, P. *Clinical Physiology* 1985; **5:** 315.

Chronic hypokalemia and intraoperative dysrhythmias. Vitez, T.S., Soper, L.E. *et al. Anesthesiology* 1985; **63:** 130.

Treatment and medication

The pacemaker syndrome. Ausubel, K., Furman, S. *Annals of Internal Medicine* 1985; **103:** 420.

Thrombolytic therapy. Bailey, A., Lydon, J.C., Spielman, F.J. *Canadian Anaesthetists' Society Journal* 1985; **32:** 385.

Office evaluation of the pacemaker patient. Bhatia, S., Goldschlager, N. *Journal of the American Medical Association* 1985; **254:** 1346.

Simple mechanical methods for cardioversion: defence of the precordial thump and cough version. Caldwell, G., Millar, G. *et al. British Medical Journal* 1985; **291:** 627.

Preventable trauma deaths. Cales, R.H., Trunkey, D.D. *Journal of the American Medical Association* 1985; **254:** 1059.

The role of stress and the sympathetic nervous system in hypertension and ischemic heart disease: advantages of therapy with beta-receptor blockers. Dequattro, V., Hamad, R. *Clinical and Experimental Hypertension. Part A—Theory and Practice* 1985; **7:** 907.

Nadolol in essential hypertension: effect on ambulatory blood pressure, renal haemodynamics and cardiac function. Dupont, A.G., Vanderniepen, P. *et al. British Journal of Clinical Pharmacology* 1985; **20:** 93.

Dopamine receptors—applications in clinical cardiology. Goldberg, L.I., Raifer, S.I. *Circulation* 1985; **72:** 245.

Enalapril: a review of human pharmacology. Gomez, H.J., Cirillo, V.J., Irvine, J.D. *Drugs* 1985; **30:** 13 (Suppl 1).

Naloxone: ineffective in improving cardiac performance after hypoperfusion in swine. Heydorn, W.H., Moores, W.Y. *et al. Circulatory Shock* 1985; **17:** 35.

Anaesthetic implications of calcium channel blockers. Jenkins, L.C., Scoates, P.J. *Canadian Anaesthetists' Society Journal* 1985; **32:** 436.

Tocainide: a new oral antiarrhythmic agent. Kutalek, S.P., Morganroth, J., Horowitz, L.N. *Annals of Internal Medicine* 1985; **103:** 387.

Intracoronary naloxone in hemorrhagic shock: dose-dependent stereospecific effects. Lechner, R.B., Gurll, N.J., Reynolds, D.G. *American Journal of Physiology* 1985; **249:** H272.

Verapamil pharmacokinetics and apparent hepatic and renal blood flow. Meredith, P.A., Elliott, H.L. *et al. British Journal of Clinical Pharmacology* 1985; **20:** 101.

Cardiovascular pathophysiology of essential hypertension: a clue to therapy. Messerli, F.H., Ventura, H.O. *Drugs* 1985; **30:** 25 (Suppl 1).

Non-invasive intermittent monitoring of blood pressure in essential hypertensives treated with enalapril. Novo, S., Alaimo, G. *et al. Current Therapeutic Research* 1985; **38:** 231.

Postoperative total parenteral nutrition in patients with liver disorders. Okuno, M., Nagayama, M. *et al. Journal of Surgical Research* 1985; **39:** 93.

Hemodynamic and humoral effects of caffeine in autonomic failure: therapeutic implications for postprandial hypotension. Onrot, J., Goldberg, M.R. *et al. New England Journal of Medicine* 1985; 549.

Analysis of morbidity and mortality in patients 70 years of age and over undergoing isolated coronary bypass surgery. Rose, D.M., Gebfish, J. *et al. American Heart Journal* 1985; **110:** 341.

Nifedipine: a review of its pharmacodynamic and pharmacokinetic properties. Sorkin, E.M., Clissold, S.P., Brogden, R.N. *Drugs* 1985; **30:** 182.

Effect of nifedipine on gastric emptying in normal subjects. Traube, M., Lange, R.C. *et al. Digestive Diseases and Science* 1985; **30:** 710.

Renin inhibitors: their use in understanding the role of angiotensin II as a pressor hormone. Tree, M., Szelke, M. *et al. Journal of Cardiovascular Pharmacology* 1985; **7:** S49.

Coronary artery bypass grafts; influence of preoperative risk factors on the late postoperative course. Tschan, W., Hoffmann, A. *et al. Chest* 1985; **88:** 185.

Pharmacological basis of the antihypertensive action of calcium entry blockers. Van Zwieten, P.A., Timmermans, P.B.M. *Journal of Cardiovascular Pharmacology* 1985; **7:** S11.

Simple method for maintaining serum lidocaine levels in the therapeutic range. Wong, B.Y.S., Hurwitz, A. *Archives of Internal Medicine* 1985; **145:** 1588.

Respiratory

Physiology

High frequency oscillation of the lungs alone lengthens expiration in dogs. Banzett, R.B., Reid, M.B., Lehr, J. *Respiration Physiology* 1985; **61:** 57.

Responses of early and late onset phrenic motoneurons to lung inflation. Donnelly, D.F., Cohen, M.I. *et al. Respiration Physiology* 1985; **61:** 69.

Changes in heart rate during breathing interrupted by recurrent apneas in humans. Findley, L.J., Farkas, G.A., Rochester, D.F. *Journal of Applied Physiology* 1985; **59:** 536.

The role of oxygen concentration in oxidative stress—hypoxic and hyperoxic models. Jones, D.P. *Oxidative Stress*. Ed. Sies, H. London: Academic Press 1985; 151.

The objective measurement of breathlessness. Killian, K.J. *Chest* 1985; **88:** 84S (Suppl).

Respiratory function in recent pulmonary sarcoidosis with special reference to small airways. Lamberto, C., Saumon, G. *et al. Clinical Respiration Physiology* 1985; **21:** 309.

Cellular and humoral mediators of pulmonary edema. Malik, A.B., Selig, W.M., Burhop, K.E. *Lung* 1985; **163:** 193.

Determinants of hypoxemia during the acute phase of pulmonary embolism. Manier, G., Castaing, Y., Guenard, H. *American Review of Respiratory Disease* 1985; **132:** 332.

Contribution of the rib cage to breathing in tetraplegia. Morgan, M.D.L., Gourlay, A.R. *et al. Thorax* 1985; **40:** 613.

Mechanical aspects of chest wall distortion. Mortola, J.P., Saetta, M. *et al. Journal of Applied Physiology* 1985; **59:** 295.

Breathing during sleep in patients with interstitial lung disease. Perezpadilla, R., West, P. *et al. American Review of Respiratory Disease* 1985; **132:** 224.

Circulating endogenous opioids and ventilatory response to CO_2 and hypoxia. Rochat, T., Junod, A.F., Gaillard, R.C. *Respiration Physiology* 1985; **61:** 85.

Calcium ions and respiratory smooth muscle function. Triggle, D.J. *British Journal of Clinical Pharmacology* 1985; **20:** 213S (Suppl 2).

Effects of high frequency ventilation on lung lymph dynamics and prostaglandin generation. Van Der Zee, H., Bizios, R., Malik, A.B. *Respiration Physiology* 1985; **61:** 31.

Respiratory changes in nasal muscle length. Van Lunteren, C., Haxhiu, M.A., Cherniack, N. *Journal of Applied Physiology* 1985; **59:** 453.

Minireview. Pulmonary antioxidant defense mechanisms. White, C.W., Repine, J.E. *Experimental Lung Research* 1985; **8:** 81.

Treatment and medication

Effect of theophylline on respiratory muscle function. Aubier, M., Roussos, C. *Chest* 1985; **88:** 91S (Suppl).

Clinical studies with calcium antagonists in asthma. Barnes, P.J. *British Journal of Clinical Pharmacology* 1985; **20:** 289S (Suppl 2).

Improved oxygenation after muscle relaxation in adult respiratory distress syndrome. Coggeshall, J.W., Marini, J.J., Newman, J.H. *Archives of Internal Medicine* 1985; **145:** 1718.

Almitrine improves oxygenation, both awake and asleep in patients with hypoxia and carbon dioxide retention caused by chronic bronchitis and emphysema. Connaughton, J.J., Douglas, N.J. *et al. American Review of Respiratory Disease* 1985; **132:** 206.

Ventilatory savings by external chest wall compression or oral high-frequency oscillation in normal subjects and those with chronic airflow obstruction. George, R.J., Winter, R.J. *et al. Clinical Science* 1985; **69:** 349.

Electrophysiologic evaluation of phrenic nerves in severe respiratory insufficiency requiring mechanical ventilation. Moorthy, S.S., Omkar, N. *et al. Chest* 1985; **88:** 211.

Use of bronchodilator aerosols. Tobin, M.J. *Archives of Internal Medicine* 1985; **145:** 1659.

Treatment of obstructive sleep apnea with continuous nasal airflow. Wilhoit, S.C., McTier, R.F. *et al. Lung* 1985; **163:** 233.

Central nervous system

Physiology

Steroids and brain function. Baethmann, A. *Brain Insults in Infants and Children: Pathophysiology and Management.* Ed. James, H.E. *et al.* 1985; 3.

The blood-brain barrier: transport across the cerebral endothelium. Bradbury, M.W.B. *Circulation Research* 1985; **57:** 213.

Pharyngeal compliance in snoring subjects with and without obstructive sleep apnea. Brown, I.G., Bradley, T.D. *et al. American Review of Respiratory Disease* 1985; **132:** 211.

Concepts of intracranial volume and pressure. Bruce, D.A. *Brain Insults in Infants and Children: Pathophysiology and Management.* Ed. James, H.E. *et al.* 1985; 19.

Cerebrovascular Dynamics. Bruce, D.A. Brain Insults in Infants and Children: Pathophysiology and Management Ed. James, H.E. *et al.* 1985; 53.

Oxidative stress in the nervous system. Cohen, G. *Oxidative Stress.* Ed. Sies, H. London: Academic Press 1985; 383.

Motor control in the spinal cord. Dimitrijevic, M.R., Faganel, J. *Recent achievements in restorative neurology.* Ed Eccles, J., Dimitrijevic, M.R. 1985; **1:** 150.

Cerebral blood flow and cognitive impairment in Parkinson's disease. Globus, M., Mildworf, B., Melamed, E. *Neurology* 1985; **35:** 1135.

Effects of prior instruction and anaesthesia on long-latency responses to stretch in the long flexor of the human thumb. Loo, K.C., McCloskey, D.I. *Journal of Physiology* 1985; **365:** 285.

Regional blood flow in hemiparkinsonism. Perlmutter, J.S., Raichle, M.E. *Neurology* 1985; **35:** 1127.

Treatment and medication

Diagnosis and management of obstructive sleep apnea. Orr, W.C., Moran, W.B. *Archives of Otolaryngology* 1985; **111:** 583.

Endocrine and metabolic

Physiology

Effects of intravenous and oral glucose administration on insulin action in human fat cells. Bolinder, J. *et al. Diabetes* 1984; **34:** 884.

Second messengers in renin secretion. Chuchill, P.C. *American Journal of Physiology* 1985; **249:** H175.

Vasopressin and plasma renin activity following disturbances in blood pressure, osmolality and/or blood volume in the fetus. Daniel, S.S., Stark, R.I. *et al. Physiological Development of the Fetus and Newborn.* Ed. Jones, C.T. and Nathanielsz, P.W. 1985; 533.

Steroid hormones, receptors and neurotransmitters. Dohanich, G., Nock, B., McEwen, B.S. *Molecular Mechanism of Steroid Hormone Action Recent Advances.* Ed. Moudgil, V.K. 1985; 701.

Changes in plasma volume, in transcapillary escape rate of albumin and in subcutaneous blood flow during hypoglycaemia in man. Hilsted, J., Bonde-Petersen, F. *et al. Clinical Science* 1985; **69:** 273.

Metabolic effects of tourniquet ischaemia studied by nuclear magnetic resonance spectroscopy. Newman, R.J. *Journal of Bone and Joint Surgery* 1984; **66:** 434.

Ketone body metabolism in normal and diabetic human skeletal muscle. Nasadini, R., Avogaro, A. *et al. American Journal of Physiology* 1985; **249:** E131.

Changes in adrenal function as a possible mechanism for elevation of serum glucose by a single large dose of fluoride. Suketa, Y., Asao, Y. *et al. Toxicology and Applied Pharmacology* 1985; **80:** 199.

Effects of naloxone-induced opiate receptors blockade on insulin secretion in obesity. Vettor, R., Martini, C. *et al. Hormone and Metabolic Research* 1985 **17:** 374.

Membrane structural studies of the action of vasopressin. Wade, J.B. *Federation Proceedings* 1985 **44:** 2687.

Treatment and medication

Hormonal effects of high dose naloxone in humans. Cohen, M.R., Cohen, R.M. *et al. Neuropeptides* 1985; **6:** 373.

Improvement of cardiovascular autonomic reflexes after amelioration of metabolic control in insulin-dependent diabetics. FEDELE, D., BELLAVERE, F. *et al.* *Hormone and Metabolic Research* 1985; **17:** 410.

Estimates *in vivo* insulin action in humans: comparison of the insulin clamp and the minimal model techniques. FOLEY, J.E., CHEN, Y.D.I. *et al.* *Hormone and Metabolic Research* 1985; **17:** 406.

Selection of patients for intensive insulin therapy. GERICH, J.E. *Archives of Internal Medicine* 1985; **145:** 1383.

Pharmacokinetics of insulin: implications for continuous subcutaneous insulin infusion therapy. KRABGEN, E.W., CHISHOLM, D.J. *Clinical Pharmacokinetics* 1985; **10:** 303.

Long-term follow-up of diabetic patients using insulin infusion pumps. LEICHTER, S.B., SCHREINER, M.E. *et al.* *Archives of Internal Medicine* 1985; **145:** 1409.

Cushing's syndrome: current status. ROSS, E.J. *Cardiology* 1985; **72:** 64.

Stop Press

Sleep and Breathing Club

The inaugural meeting of this group, which is intended to bring together all those people interested in sleep-disordered breathing will take place at the Postgraduate Medical Centre, The Royal Infirmary, Leicester on April 15 1986. Further information can be obtained from Dr C.D. Hanning, Department of Anaesthesia, The General Hospital, Leicester, LE5 4PW.

Correction

Anaesthesia, 1985, Volume 40, pages 1231–1247

Owing to an oversight, the qualifications of Drs J.B. White and L.C. Twohey were transposed in the contents page of the Correspondence section.

Notice to contributors to *Anaesthesia*

Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Articles accepted become copyright of *Anaesthesia*.

Contributors are requested to submit two copies of manuscripts. They are also advised to retain a third copy as the Editors cannot accept responsibility for the loss of manuscripts in the post. The covering letter should be signed personally by all the authors and careful consideration should be given to the decision to include more than five authors. Articles should be forwarded to:

Dr J. N. Lunn, Editor of ***Anaesthesia****, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.*

PREPARATION OF MANUSCRIPTS

Articles for *Anaesthesia* should be prepared in accordance with *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5) except that the titles of journals in the reference section should be given in full (see below). A reprint of these requirements of which this notice is a summary, can be obtained from the *British Medical Journal* price 50 pence (U.K.).

Type manuscripts on white bond paper, 20.3 × 26.7 cm or 21.6 × 27.9 cm (8 × 10½ in. or 8½ × 11 in.) or ISO A4 (212 × 297 mm) with margins of at least 2.5 cm (1 in.). Use double, and preferably triple, spacing throughout, including the references. Please do not use a dot matrix printer, particularly one with poor quality descenders or ascenders. Unseparated, fan-folded manuscripts may be returned to the author.

The manuscript should consist of the following sections in this order each beginning on a new page: *title page*, *summary* and *key words*, *text*, *acknowledgments*, *references*, *individual tables*, and *legends for figures*.

Number pages consecutively, beginning with the title page. Type the page number in the upper right-hand corner of each page.

THE TITLE PAGE

The name of the author and the address to which proofs and other correspondence is to be addressed should appear in the top left-hand corner of the sheet.

The main title should be restricted to five words if this is possible. It should be typed in capitals across the centre of the title page.

A subsidiary title of not more than 12 words may be supplied if this is considered to be necessary. This should be typed in lower case immediately beneath the main title.

The names of the authors should be typed IN CAPITALS across the title page immediately beneath the titles without degrees or designations. Initials should precede the surname. One forename may be given in full according to the author's preference. If there is more than one author the word 'AND' should be placed before the name of the last author.

A line should be typed across the title page below the author(s) name(s) in capitals.

The author(s) name(s) degrees and designations should be typed in lower case below the line. Initials and/or forename should precede the name of each author and his degrees, without full stops between letters, and appointment (e.g. Consultant, Registrar, etc.) should follow it.

A full postal institutional address should follow the names, degrees and appointments. Correspondence will normally be addressed to the first author but, if it is desired to direct correspondence other than to the first author, or if different authors belong to different institutions or departments, a separate sentence should be added; this should start on a new line and begin 'Correspondence should be addressed to ...' and a full postal address should follow.

SUMMARY AND KEY WORDS

Start a new sheet

The second page should carry a summary of not more than 150 words. The summary should state the purpose of the study or investigation, basic procedures, main findings and their statistical significance, and the principal conclusions.

Do not use abbreviations except for units of measurement (e.g. mg, cm, etc.).

Key (indexing) words. Below the abstract, provide and identify as such, three to 10 key words or short phrases that will assist indexers. Use terms from the Medical Subject Headings list from *Index Medicus*. The Editor may modify these at proof stage to conform with agreed practice of certain other anaesthetic journals in the English language.

COPYRIGHT OFFPRINTS

Authors submitting a manuscript do so on the understanding that if it is accepted for publication, exclusive copyright in the paper shall be assigned to the Association. In consideration for the assignment of copyright, the Publisher will supply 25 offprints of each paper. Further offprints may be ordered at extra cost; the copyright assignment form and the offprint order form will be sent with the proofs. The Association will not put any limitation on the personal freedom of the author to use material contained in the paper in other works.

(continued overleaf)

THE TEXT

Start a new sheet

The text of observational and experimental articles, case reports, etc. is usually divided into sections with the headings *Introduction, Methods, Results* and *Discussion.* Long articles will need subheadings within some sections to clarify their content.

Letters for the correspondence pages should be double spaced and prepared in accordance with the format in a recent copy of *Anaesthesia.*

Headings: three steps of heading may be used in typescripts:

(i) CAPITALS across the centre of the page.

(ii) Underlined words

These should be typed at the left hand side of the page above the paragraph which they precede.

(iii) Underlined words at the beginning of a paragraph. These may either be followed by a full stop or form part of the first sentence of the paragraph.

ACKNOWLEDGMENTS

Start a new sheet

Acknowledge those who have made substantive contributions to the study or the preparation of the manuscript. Authors are responsible for obtaining written permission for publication of reproduced figures and tables from authors and publishers and from everyone acknowledged by name because of copyright conventions and because readers may infer their endorsement of the data and conclusions.

REFERENCES

Start a new sheet

Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by arabic numerals. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. Use double or treble space typing.

Use the form of reference adopted by the U.S. National Library of Medicine and used in *Index Medicus.* Use the style of the examples cited at the end of this section.

The titles of journals should be given in full.

Avoid using abstracts as references except those published in a recognised journal. 'Unpublished observations' and 'personal communications' may not be used as references, although references to written, not verbal, communications may be inserted (in parentheses) in the text. Include among the references manuscripts accepted but not yet published; designate the journal followed by (*in press*) in parentheses. Information from manuscript submitted but not yet accepted should be cited in the text as (unpublished observations) in parentheses.

The references must be verified by the author(s) against the original documents.

Examples of correct form of references

Note: first and last pages in all references.

JOURNAL

Standard journal article—(List all authors)

SOTER NA, WASSERMAN SI, AUSTEN KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294:** 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

OSLER AG. *Complement: mechanisms and functions.* New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. AMA drug evaluations. 3rd ed. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

RHODES AJ, VAN ROOVEN CE, *comps. Textbook of virology; for students and practitioners of medicine and other health sciences.* 5th ed. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

WEINSTEIN L, SWARTZ MN Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease.* Philadelphia: WB Saunders, 1974: 457–72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, Md: National Center for Health Statistics, 1972. (*Vital and health statistics. Series* **10:** Data drom the National Health Survey, No. 69) [DHEW publication No. (HSM) 72–1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

ROUECHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

TABLES

Do not include tables in the text. Start a new sheet for each table and space the material adequately. The author(s) name(s) should appear in the top right-hand corner.

Indicate the approximate position of each table in relation to the subject matter of the text in the right-hand margin of the appropriate page on the manuscript. Do not submit tables as photographs. Number tables consecutively with arabic numerals. Supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes. Explain in footnotes all non-standard abbreviations that are used in each table. For footnotes, use the following symbols in this sequence: *, †, ‡, §, ||, ¶, **, ††, etc. Identify statistical measures of variations such as SD and SEM. *Legends for tables* should appear on the face of the table.

Cite each table in the text in consecutive order and mark the approximate position of the table in the right-hand margin of the text.

FIGURES

Each figure should be separate. Do not include figures in the text but collect together in an envelope or folder.

Indicate the approximate position of each figure in relation to the subject matter of the text in the right-hand margin of the appropriate page of the manuscript. Drawings, charts and diagrams should be submitted in black indian ink on a smooth white card and should be about twice the size of that desired in the published version with no lettering. Full plate, glossy black and white photographs will be accepted if they are sufficiently clear. All letters and numerals required on the face of figures must be clearly typed or written on tracing paper firmly attached with self-adhesive tape to the back of the figure and folded over from the front as a cover. They will then be printed in the style of *Anaesthesia* in the exact location indicated. Identify each figure by its sequential number in pencil on the reverse of the illustration and include the title of the paper and the authors' names. Mark the top of the illustration on the reverse by an arrow and the word 'Top'.

All sources of identification of patients must be removed.

LEGENDS FOR FIGURES

Start a new sheet

Type legends for illustrations double spaced with arabic numerals corresponding to the illustrations. When symbols, arrows, numbers or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

CONVENTIONS AND ABBREVIATIONS

Statistics and measurements should be given in figures except that numerals one to nine should be in words if not followed by a measurement symbol (e.g. 'two patients' but '2.0 mg'). The *Système International* (SI) will usually be used except that vascular pressures will be recorded in mmHg and cmH_2O. Imperial measurements will not be used except in an historic context. The 24 hour clock will be used.

Contributors are advised to study the SI *Conversion Tables* provided in the January 1978 issue of *Anaesthesia, Units, Symbols and Abbreviations* (*A Guide for Biological and Medical Editors and Authors*) published by the Royal Society of Medicine, London W1M 8AE, and *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5).

LETTERS FOR PUBLICATION

Should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University of Wales Hospital, Heath Park, Cardiff CF4 4XW, UK.

Letters should be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters above. The degrees and diplomas of each author must be given in a covering letter which must be signed personally by all the authors.

Correspondence presented in any other style or format may be the subject to considerable delay and may be returned to the author for revision.

The editors regret that failure to comply with the above requirements may result in a delay in publication of accepted papers.

REVIEW JOURNALS

This journal is covered by *Current Contents*, *ASCA* and the *Science Citation Index*.

Contents: Anaesthesia, vol. 41, no. 3, March 1986

EDITORIAL

A crisis of learning in anaesthesia
R.D. Jack 241

ORIGINAL ARTICLES

Plasma cholinesterase changes during the puerperium
N. Robson, I. Robertson and M. Whittaker 243

Diabetes mellitus and open heart surgery. A simple, practical closed-loop insulin infusion system for blood glucose control
B.G. Watson, M.J. Elliott, D.A. Pay and M. Williamson 250

Anxiety levels in junior anaesthetists during early training
C.A. Pinnock, A.E. Elling, R.J. Eastley and G. Smith 258

Meptazinol versus pethidine for postoperative pain relief in children
S.A. Ridley, N.C. Matthews and J. Dixon 263

Influence of induction of anaesthesia with midazolam on the neuro-endocrine response to surgery
D. Dawson and J.W. Sear 268

Blood glucose in anaesthetised children. Comparison of blood glucose concentrations in children fasted for morning and afternoon surgery
N. Redfern, G.M. Addison and G. Meakin 272

Midazolam in conservative dentistry. A cross-over trial
R.A. Dixon, C. Kenyon, D.R.G. Marsh and J.A. Thornton 276

Intubating conditions following pre-induction priming with alcuronium
A.W. Harrop-Griffiths, R.M. Grounds and M. Moore 282

Pressure changes in tracheal tube cuffs
M. Chandler 287

The stability of preservative-free morphine in plastic syringes
R.J. Bray, P.A. Davies and J.A. Seviour 294

CASE REPORT

Anaesthesia for Friedreich's ataxia. Case report and review of the literature
C.F. Bell, J.M. Kelly and R.S. Jones 296

APPARATUS

The Nellcor N-101 pulse oximeter. A clinical evaluation in anaesthesia and intensive care
J.A. Tytler and H.F. Seeley 302

Force exerted by epidural catheters
P.A.J. Hardy 306

Halothane and trichloroethylene. Two agents in a single vaporizer
N. Hollis 309

Clinical automatic control of neuromuscular blockade
A.J. Asbury and D.A. Linkens 316

CORRESPONDENCE 321

BOOK REVIEWS 339

ANAESTHETIC LITERATURE 343

STOP PRESS 349

CORRECTION 349

Printed in Great Britain by Fletcher & Son Ltd, Norwich

Acc.
25.9.87

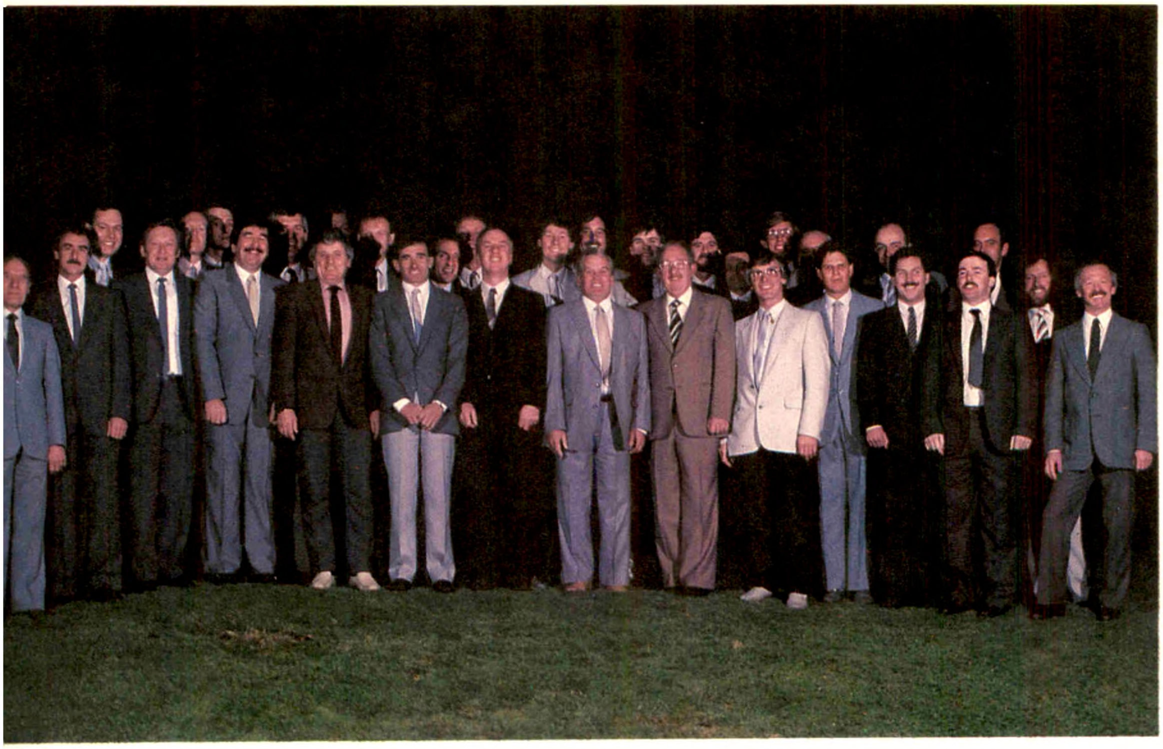
Anaesthesia

Journal of the Association of Anaesthetists of Great Britain & Ireland

Volume 41 Number 4 April 1986

Published for
The Association of Anaesthetists of Great Britain and Ireland by
Academic Press Grune & Stratton
London Orlando San Diego New York Toronto
Montreal Sydney Tokyo

ISSN 0003-2409



Eighty more good reasons to specify Ohmeda

From the day you decide on Ohmeda equipment our Service Department takes full responsibility for installation, testing and regular planned maintenance. In short, total responsibility for keeping your equipment working at peak performance.

To provide this level of back-up, in addition to the factory-based Technical Support Department, we run a UK service network of more than 80 Field Engineers and Service Supervisors. People who are trained to care for the electronics as well as the mechanics of Ohmeda equipment.

Responding into 5 Regional Offices, and easily contacted by radio-pagers, our engineers work wherever your equipment is installed – in ambulances, on oil rigs, as well as in hospitals, dental surgeries and industrial locations.

But there is more to service than turning up when you need us. There is a turning up when you don't think you need us. Through Ohmeda's planned service policy, key machine parts are automatically replaced at regular intervals to ensure optimum performance is always maintained. Its all part of Ohmeda's policy of putting safety first.

SPECIALIST CARE FOR SPECIALIST PRODUCTS.

Ohmeda

Ohmeda
Elizabeth Way Harlow Essex CM19 5AB England
0279 29692 Telex 81497

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

Editorial Board
Editor J. N. LUNN
Assistant Editors M. MORGAN, C. E. BLOGG, R. GREENBAUM, R. M. JONES
Chairman P. J. HELLIWELL
Advisory Editors R. S. ATKINSON, T. B. BOULTON
Members C. F. SCURR, P. J. F. BASKETT, D. J. HATCH and a representative of the Junior Anaesthetists Group
Ex officio
The President of the Association T. B. BOULTON
The Honorary Treasurer of the Association M. M. BURROWS
The Honorary Secretary of the Association M.T. INMAN
The Assistant Honorary Secretary of the Association P. MORRIS

Editor Emeritus C. LANGTON HEWER

Sub-editors of special sections
L. KAUFMAN Anaesthetic literature
A. PADFIELD National and local events
G. D. PARBROOK Audiovisual reviews
M. J. HARRISON Computer programs
JACQUELINE WELCH, DIANE WINTERBURN Reference librarians
D. V. BATEMAN Honorary proof reader

Address for literary contributions Dr J. N. Lunn, The Editor, *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK [telephone Cardiff (0222) 763601; Ansafone available].

Neither the Editor nor the Association of Anaesthetists of Great Britain and Ireland is in any way responsible for the statements made or the views expressed by contributors.
Investigations performed on man must conform to appropriate ethical standards including voluntary consent and acceptance by an ethical committee.

Published monthly (January–December) at 24–28 Oval Road, London NW1 7DX, England by Academic Press Inc. (London) Limited for the Association of Anaesthetists of Great Britain and Ireland, Rooms 475–478, Tavistock House South, Tavistock Square, London WC1H 9LG. As from December 2nd 1985, 9 Bedford Square, London WC1B 3RA

1986, Volume 41, 12 issues. Inland £80.00 inclusive of postage and packing; abroad, $189.00 inclusive of postage and packing. Subscription orders should be sent to Academic Press Inc. (London) Limited, High Street, Foots Cray, Sidcup, Kent DA14 5HP (Tel. 01-300-0155). Send notices of change of address to the office of the Publishers at least 6–8 weeks in advance. Please include both old and new addresses

Application to pay at second class postage rates pending at Jamaica, New York 11431, U S A

Air freight and mailing in the U S A by Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, U S A

© 1986 The Association of Anaesthetists of Great Britain and Ireland. The appearance of the code at the bottom of the first page of a paper in this journal indicates the copyright owner's consent that copies of the paper may be made for personal or internal use, or for the personal or internal use of specific clients in the U S A. This consent is given on the condition, within the U S A., that the copier pay the stated per-copy fee through the Copyright Clearance Center Inc., 27 Congress Street, Salem, MA 01970, U S A for copying beyond that permitted by Sections 107 or 108 of the U S Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, for resale or for copying or distributing copies outside the U S A

ISSN 0003-2409

LIBRARY ... OF MEDICINE

NEUROSTIM LA II

The new stimulator for successful peripheral nerve blockade.

Tracing of the nerves without injury!

The metallic tip of the plastic-coated unipolar needle has to be inserted so close to the nerve that at a stimulus amplitude of 0.5 mA muscle contractions still occur. Thus the tip of the needle is so close to the nerve that already small dosages of local anaesthetic show sufficient effect. The Neurostim LA II is also an excellent tool for tracing peripheral nerves during pain treatment.

Unipolar cannulas – plastic-coated – are available in 4 lengths (40, 80, 120 and 180 mm).

Please ask for literature!

We will exhibit at the Regional Anaesthesia Meeting in San Antonio, USA, March 20–23, 1986, booth No. 9

HUGO SACHS ELEKTRONIK KG
D–7806 March-Hugstetten, Fed. Rep. Germany
P.O. Box 9. Telex 7722929 hse d

HSE

Muscle Relaxation Based on the Patient's Needs

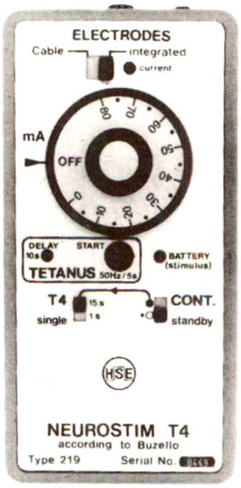
How to tailor the individual dose?
Adequate Muscle Relaxation?
Phase II Block?
Neuromuscular Pathology
    Patient ready for extubation?
    Continuing mechanical ventilation?
Relaxant Hangover?
Narcotics Hangover?
May a reversal agent be used safely?

One answer to many questions

NEUROSTIM T4

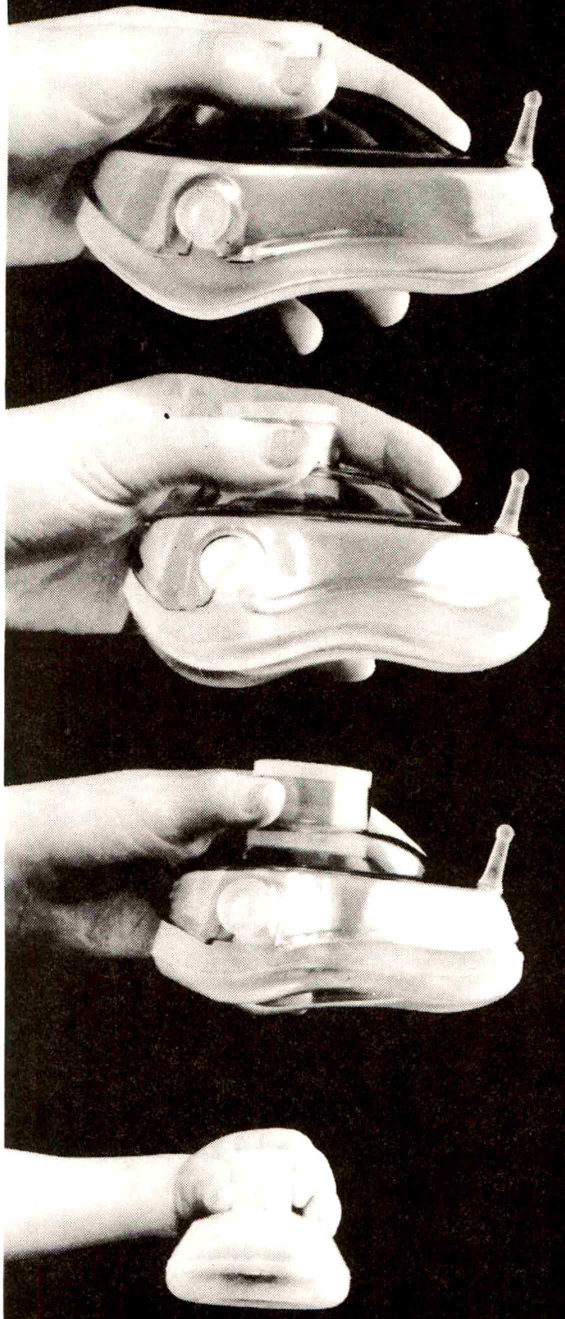
. . . for monitoring muscle relaxation
the constant current nerve stimulator

simple – safe – reliable



HUGO SACHS ELEKTRONIK KG,
D–7806 March. Fed. Rep. Germany
P.O. Box 9. Telex 7722929 hse d

HSE



LAERDAL SILICONE MASKS

for Anaesthesia, Resuscitation and Respiratory Therapy

IMPORTANT FEATURES

Transparent domes
Easy monitoring of lip colour and presence of vomitus.

Contoured pliable mask rims
Airtight and comfortable seal with a minimum of pressure.

Small external measurements
Easy to hold even for operators with small hands. Comfortable grip reduces hand fatigue.

Soft mask port bushings
Quick and safe attachment to gas delivery equipment. Will adapt to the small variations often found in connector diameter and tapering.

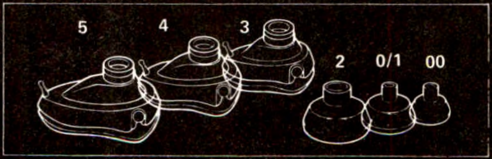
SUPERIOR ECONOMY

Can be re-used hundreds of times
Hard polysulfone and soft silicone parts will accept all commonly used methods of disinfection and sterilization, including pasteurization, boiling, gas sterilization and steam autoclaving up to 136°C (277°F).

Can be stored almost indefinitely
Materials and manufacturing provide extremely long shelf life.

All-purpose suitability
allows standardization in purchasing, inventory and cleaning.

FULL RANGE OF SIZES



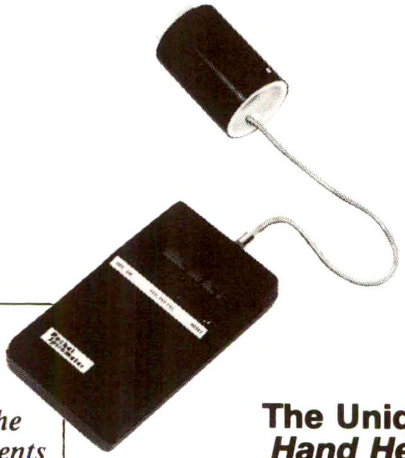
Large adult (5), small adult (4), child (3) masks have rigid domes and soft rims and mask port bushings. Infant sizes (00, 0/1, 2) are made in one soft silicone rubber piece.

Laerdal Medical Ltd.
TRAINING AIDS and MEDICAL EQUIPMENT

Laerdal Medical Limited
Laerdal House
Goodmead Road
Orpington
Kent BR6 0HX
Tel. Orpington: (0689) 76634
Telex: 8955251 LML G

Pocket Spirometer

- ☐ **INEXPENSIVE**
- ☐ **ACCURATE**
- ☐ **PORTABLE**
- ☐ **PEAK FLOW**
- ☐ **FEV$_1$**
- ☐ **FVC**



Now Available with Printer Output for Hardcopy of Data and Volume Time Curve using the new Micro Medical Instruments Pocket Printer.

The Unique *Hand Held* Spirometer

For more information on the Micro Medical Instruments Pocket Spirometer and our other respiratory products contact:-

micro Medical Instruments

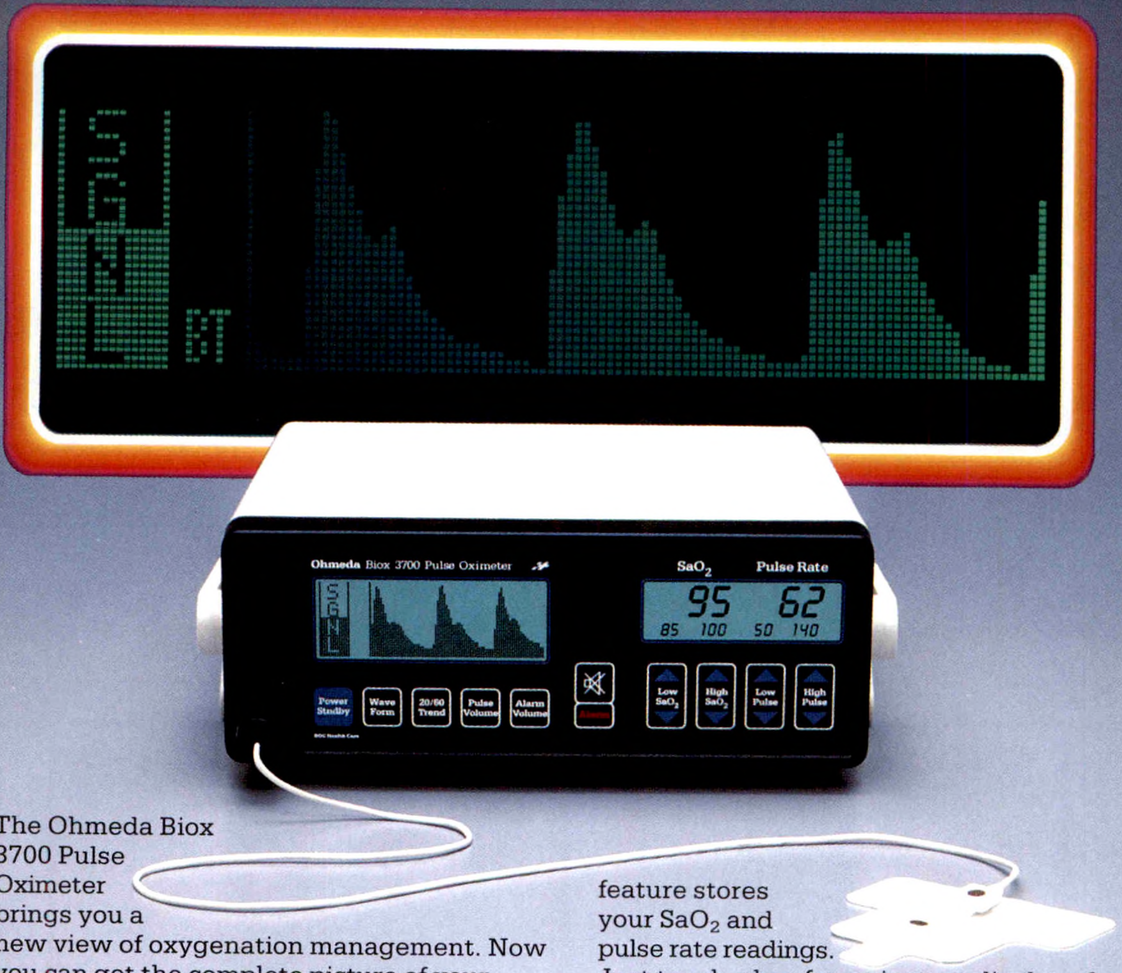
Micro Medical Instruments,
P.O. Box 6, Rochester, Kent.
ME1 2AZ, ENGLAND.
Telephone: Medway (0634) 712290

Hespan

Hetastarch 6%

In place of plasma in hypovolaemia

Further information is available on request
American Hospital Supply (U.K.) Ltd.
Wallingford Road, Compton, Nr. Newbury,
Berkshire RG16 0QW.



A New Perspective

The Ohmeda Biox 3700 Pulse Oximeter

The Ohmeda Biox 3700 Pulse Oximeter brings you a new view of oxygenation management. Now you can get the complete picture of your patient's SaO_2 and pulse status. Through the continuous Plethysmographic Display and Trend Memory, crucial information is available immediately to aid in patient management decisions.

Plethysmographic Display and Trend Memory. World First in oximetry, only from Ohmeda.

The 3700's **Plethysmographic Display** allows you to see beat-by-beat blood volume changes. A **Signal Strength Indicator** alongside the graph measures the signal quality at the probe site. A **Trend Memory** feature stores your SaO_2 and pulse rate readings. Just touch a key for an instant display of oxygenation patterns over 20 or 60 minutes. Recording is easily accessed through analog or digital outputs. Continuous internal memory holds up to 8 hours of saturation and pulse data automatically.

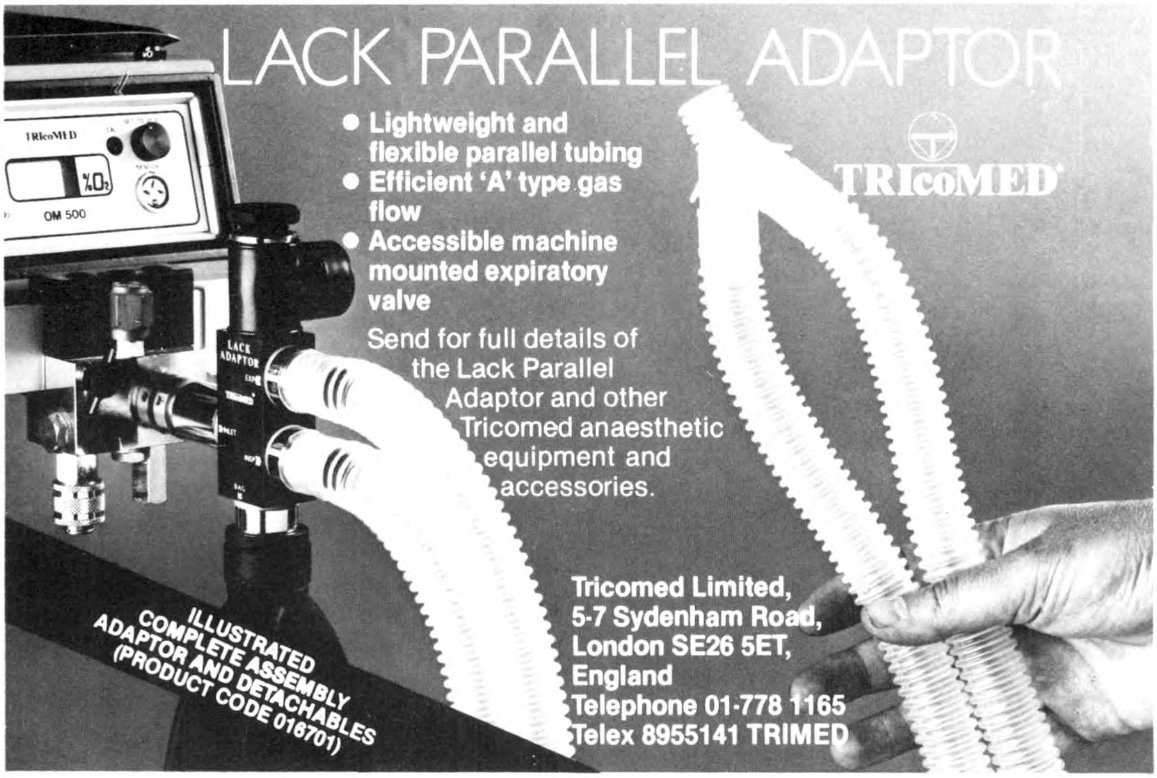
There has never been a more thorough or convenient oxygenation monitoring tool.

More options than ever before. Only the Ohmeda Biox 3700 gives you three versatile probe options; ear, fingertip, and a new flex probe for neonatal as well as adult application. The Ohmeda Biox 3700—it's the practical innovation you expect from world leaders in oximetry.

Ohmeda

Ohmeda
4765 Walnut Street Boulder, Colorado 80301
Telephone 303 447 9842 Telex 296445 BTI UR

Ohmeda
Elizabeth Way
Harlow, Essex CM19 5AB England



LACK PARALLEL ADAPTOR

- Lightweight and flexible parallel tubing
- Efficient 'A' type gas flow
- Accessible machine mounted expiratory valve

Send for full details of the Lack Parallel Adaptor and other Tricomed anaesthetic equipment and accessories.

TRIcoMED

ILLUSTRATED COMPLETE ASSEMBLY ADAPTOR AND DETACHABLES (PRODUCT CODE 016701)

Tricomed Limited,
5-7 Sydenham Road,
London SE26 5ET,
England
Telephone 01-778 1165
Telex 8955141 TRIMED

AUTOMATIC TOURNIQUET

For ANTIGRAVITY SUIT inflation
ORTHOPAEDIC SURGERY
REGIONAL ANAESTHESIA
– Bier's Block
with comprehensive range of cuffs and accessories

SCHUCO INTERNATIONAL LONDON LTD
Woodhouse Road, London N12 0NE
Tel: 01 368 1642

NEW from CDL

SILICONE RENDELL BAKER CHILDREN'S MASK

The mask for children with minimum dead-space achieved by anatomically correct shape.
Made of soft translucent autoclavable elastomer with 22mm B.S. fitting.
Sizes: 0, 1, 2 & 3

CHILDERHOUSE DEVELOPMENTS LTD
310A Upper Richmond Road West
London SW14 7JN Tel: 01 876 4078

WE'VE
GIVEN YOU
PRECISELY
WHAT YOU
WANTED

MORE
DILUTE
HYPNOVEL

When we asked how Hypnovel could be improved, many users asked for a more dilute presentation, so that finer control of dosage, and therefore sedation, could be achieved. So the 2ml presentation was joined by an ampoule containing the same 10mg of midazolam, but in 5ml of solution. The extra 3ml of diluent makes it simpler to obtain the full benefits of Hypnovel. Proven benefits of Hypnovel include fast onset and rate of recovery, excellent amnesia and minimal venous complications.[1]

THE
HYPNOVEL 10mg/5ml
midazolam AMPOULE

FOR MORE PRECISE
CONTROL OF I.V. SEDATION

Prescribing Information

Indications Intravenous sedative cover. Alternative intravenous agent for induction of anaesthesia in high-risk patients. Intramuscular premedication. **Dosage and Administration** *Intravenous sedation* Usual total dose 2.5mg to 7.5mg (approx. 0.07mg/kg body-weight). *Intravenous induction of anaesthesia* Unpremedicated patients: 0.3mg/kg body-weight or more. Premedicated patients: 0.2mg/kg body-weight may be adequate. *Intramuscular premedication* (10mg/2ml ampoule only) Usual dose about 5mg (approx. 0.07-0.1mg/kg body-weight). Elderly patients are more sensitive to the effects of Hypnovel and lower doses should be used. Children over the age of seven years may receive Hypnovel for induction of anaesthesia in a dose of 0.15mg/kg body-weight. **Contra-indications** Benzodiazepine sensitivity; acute pulmonary insufficiency; respiratory depression. **Precautions** Use during pregnancy and lactation should be avoided. Patients should not drive or operate machinery for eight hours after administration. Avoid alcohol. Sedative effects of other centrally-acting drugs may be intensified. For the administration of Hypnovel a second person should always be present and facilities for resuscitation should always be available. **Side-effects** Hypnovel is well tolerated and changes in arterial blood pressure, heart rate and respiration are usually slight. The rapid injection of a high dose can induce soft-tissue airway obstruction or apnoea of short duration. Local effects on veins are infrequent. However, pain on injection and thrombophlebitis may occur. **Presentation** Ampoules containing 10mg midazolam base as the hydrochloride in 5ml or 2ml aqueous solution, in packings of 10. **Basic NHS Cost** 76p per 10mg/5ml ampoule. 64p per 10mg/2ml ampoule. **Product Licence Numbers** 0031/0189 (10mg/5ml), 0031/0126 (10mg/2ml). **Product Licence Holder** Roche Products Limited, PO Box 8, Welwyn Garden City, Hertfordshire AL7 3AY. **Reference** 1. Anaesthesia. 1982, **37**, 1002.
Hypnovel is a trade mark.

ROCHE

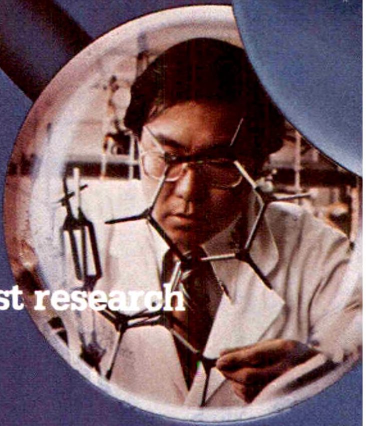
1391096/286

AErrane™ (isoflurane)

A Complete Anaesthetic

- **With or without premedications, relaxants or nitrous oxide,** AErrane™ (isoflurane) suppresses consciousness, pain, muscle tone, and memory of the operation.
- **Inhalational control is enhanced by a low solubility in blood.**
- **Muscle relaxation with AErrane™ (isoflurane) alone is sufficient for most surgical needs;** supplemental relaxant requirement is markedly reduced or eliminated (as is the need for reversal agents postoperatively).
- **Relaxation of the chest wall and diaphragm permits easily assisted or controlled ventilation without concern for "stiff chest."** Respiratory depression dissipates promptly with recovery.
- **AErrane™ (isoflurane) is the most rapidly eliminated of all potent modern anaesthetics,**[1] thus providing for a prompt, smooth recovery, with few post-anaesthetic sequelae.

Please contact your Anaquest representative or our offices to arrange for AErrane™ (isoflurane) vaporisers.



AErrane™... a product of original Anaquest research (isoflurane)

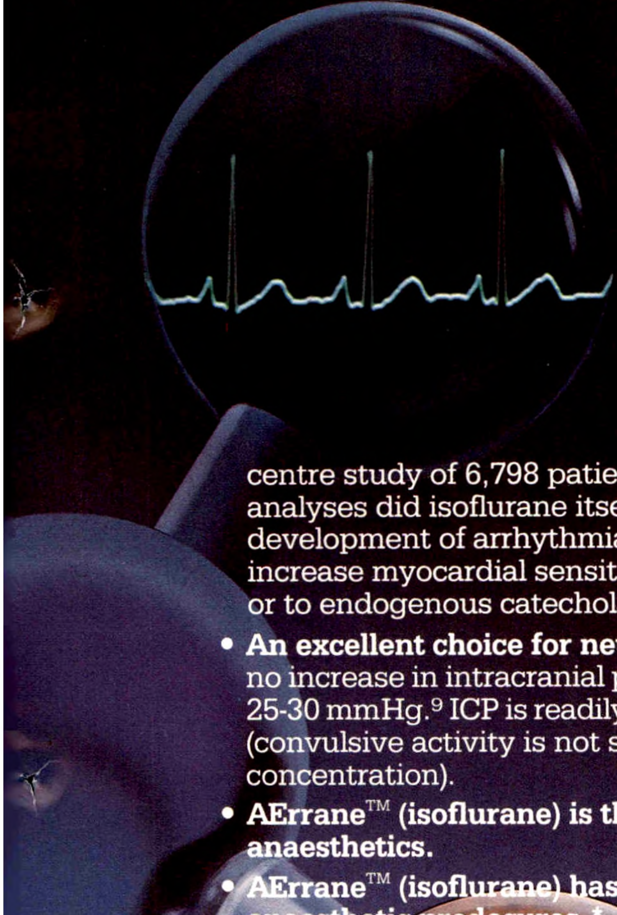
Anaquest

The Dorcan Complex
Faraday Road
Swindon Wiltshire SN3 5JB
United Kingdom
0793 615581

Corrig Road
Sandyford Industrial Estate
Dublin 18 Ireland
01 953421

For the Sum of Your Patient's Anaesthetic Needs

Intraoperative Margins of Safety



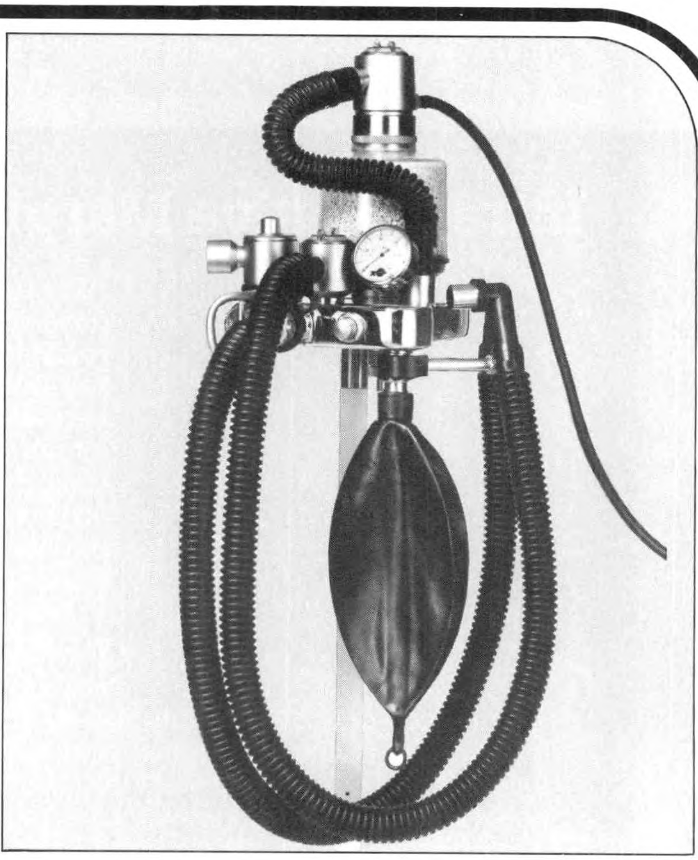
- **AErrane™ (isoflurane) causes a dose-related decrease in peripheral resistance (and cardiac afterload) but little or no depression of myocardial function or cardiac output** (at normal levels of surgical anaesthesia, 1 to 1.5 MAC).[2] These effects are potentially useful in the elderly;[3] in patients with coronary artery disease,[4] and for induced hypotension in cerebral aneurysm surgery.[5]
- **Cardiac rhythm tends to remain stable.** A report from a large multicentre study of 6,798 patients states, "In none of the extensive analyses did isoflurane itself appear to be a factor associated with development of arrhythmias."[6] AErrane™ (isoflurane) also does not increase myocardial sensitivity to adrenalin[7] used for haemostasis or to endogenous catecholamines.[8]
- **An excellent choice for neurosurgery,** AErrane™ (isoflurane) causes no increase in intracranial pressure (ICP) when $PaCO_2$ is controlled at 25-30 mmHg.[9] ICP is readily lowered at any time by decreasing $PaCO_2$ (convulsive activity is not seen at any $PaCO_2$ level or anaesthetic concentration).
- **AErrane™ (isoflurane) is the least metabolized of all potent anaesthetics.**
- **AErrane™ (isoflurane) has been used in more than 20 million anaesthetic prodecures.***

*AErrane™ (isoflurane) is not approved for use in obstetrics.

REFERENCES: 1. Cromwell TH, et al: Forane uptake, excretion and blood solubility in man. Anesthesiology 35:401-408, 1971. 2. Stevens WC, et al: The cardiovascular effects of a new inhalation anesthetic, Forane, in human volunteers at constant arterial carbon dioxide tension. Anesthesiology 35:8-16, 1971. 3. Linde HW, et al: Cardiovascular effects of isoflurane and halothane during controlled ventilation in older patients. Anesth Analg 54:701-704, 1975. 4. Mallow JE, et al: Hemodynamic effects of isoflurane and halothane in patients with coronary artery disease. Anesth Analg 55:135-138, 1976. 5. Lam AM, et al: Cardiovascular effects of isoflurane-induced hypotension for cerebral aneurysm surgery. Anesth Analg 62:742-748, 1983. 6. Levy W: Clinical evaluation of isoflurane: Cardiac arrhythmias. Can Anaesth Soc J 29 (suppl): 828-834, 1982. 7. Johnston RR, et al: A comparative interaction of epinephrine with enflurane, isoflurane and halothane in man. Anesth Analg 55:709-712, 1976. 8. Suzukawa M, et al: Use of isoflurane during resection of pheochromocytoma. Anesth Analg 62:100-103, 1983. 9. Adams RW, et al: Isoflurane and cerebrospinal fluid pressure in neurosurgical patients. Anesthesiology 54:97-99, 1981.

Prescribing Information. Indications: For general anaesthesia. **Dose:** Inspired concentrations of 1.5 to 3.0% AErrane produce surgical anaesthesia in 7 to 10 minutes. Surgical anaesthesia can be maintained with 1.0 to 2.5% AErrane when used concomitantly with nitrous oxide. **Contraindications:** Known sensitivity to AErrane or other halogenated anaesthetics; known or suspected genetic susceptibility to malignant hyperthermia. **Side Effects:** Hypotension, respiratory depression, arrhythmias, elevated white blood count, shivering, nausea, vomiting and ileus have been reported. **Product Licence Number:** 5247/0002.

A New Concept in Anaesthesia



The Ruben Circle

An anaesthesia system which is both open and closed at the same time.

- No spill valve adjustments
- No adjustment when changing between spontaneous controlled and assisted ventilation
- Fresh gas consumption extremely low
- No risk of pressure build-up
- Pollution risk eliminated
- Conforms to ISO standards

Ambu®

Ambu International · Søndre Ringvej 49 · DK-2600 Glostrup-Copenhagen · Denmark
Ambu International U.K. Ltd, Charlton Road, Midsomer Norton, BATH BA3 4DR. Telephone: (0761 416868)

Anaesthesia, 1986, Volume 41, pages 351–352

Editorial

Adverse reactions to drugs and anaesthetists

The Committee on Safety of Medicines (CSM) is a government organisation in the United Kingdom similar to that of the Federal Drug Administration in the United States of America: the remits of both of these organisations include the overall safety of drugs. The CSM has a system of reporting of adverse reactions to any drugs by any doctor; this is based on confidential reports known as yellow cards.

Anaesthetists were the first specialty to receive a letter of warning from the CSM, based on yellow card reports. Dated 5 January 1974, this was titled 'Jaundice following repeat exposure to halothane'. It concluded that, 'The Committee recognise that widespread experience over many years has demonstrated the value of halothane as an anaesthetic. They have, however, encouraged the authors to publish their findings so that anaesthetists might be made aware of this additional evidence when assessing all the relative risks of the various anaesthetic agents in the clinical circumstances of each case.'

This warning letter was similar in its content to the report of Inman and Mushin published in the same week in the British Medical Journal.[1] This was primarily intended to guide anaesthetists in their choice of drugs for repeat anaesthetics, but subsequent correspondence to medical journals showed that it was not appreciated by the specialty, although a few anaesthetists clearly understood its message. In retrospect, one has to realise what a boon halothane had become to anaesthetists; it was easy to administer and allowed rapid change in depth of anaesthesia, trichloroethylene being the only widely used nonflammable alternative. There were some correspondents who saw this either as a form of dictatorship or who doubted the scientific value of the reports received. Clearly, many had not used this means of reporting adverse effects of drugs.

It may have been a coincidence, or evidence of a lack of confidence between anaesthetists and the drug regulatory authorities, but the next (and to date the largest) report of side effects of drugs was a joint venture by an academic department and a pharmaceutical company.[2] This highlighted the anaphylactoid response to intravenous anaesthetics, something of which we have become very aware since the loss of Althesin and Epontol. Of the 100 adverse reports analysed, only 17 had been reported to the CSM. Even then it was clear that there was gross underreporting of adverse reactions to the CSM by anaesthetists.

Side effects of drugs is a topical issue and receives much attention by the media. The most outstanding example is what has been referred to as the 'Opren scandal': an alleged delay in the removal of a nonsteroidal anti-inflammatory drug from clinical use was blamed by some for deaths, particularly in the elderly.

While side effects of anaesthetic drugs are frequently described in the anaesthetic journals, why is there this low reporting to the official channels? Anaesthetists, who actually *give* more drugs than any other physician, have some specific problems in reporting side effects, which do not apply to the same extent to other specialties, although they apply to those working in intensive therapy units or casualty departments. There can be difficulty in recognising an abnormal reaction and appreciating its significance. No other specialty sees as much hypotension or apnoea without alarm and to distinguish between the normal and abnormal is not always easy. There is the problem of motivation to report any incident—why bother?—it will make no difference! Others may leave this to the academics or to their juniors. A small minority may have problems of honesty in assessing the situation and resulting troublesome thoughts on possible medicolegal implications. However, they can be assured of the confidentiality of the reports sent to the CSM.

More important are the logistic problems of completing the yellow cards. Many anaesthetists work single-handedly, some have multiple sites of work, with morning and afternoon sessions in different

0003–2409/86/040351 + 02 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

hospitals or different theatres in the same hospital. The heavy work schedule of some does not allow time to complete records between cases, without disruption of the operating session. This contrasts with the more leisurely work schedule of most physicians or family practitioners, who contribute the majority of reports. These usually have ready access to secretarial help and most have offices, while there are anaesthetists who are fortunate even to have a locker.

Nor are the existing yellow cards themselves free from problems. Firstly, there are the practical problems of where to store them, so as to be immediately available when required. Theatre sisters and hospital pharmacists could play a useful part here, but some do not appear to be willing to cooperate (or perhaps they have not had the problem explained properly).

Finally, there is a pressing question: is the yellow card, as at present designed, suitable for use in an emergency? Most anaesthetists would agree that they need something more relevant to their situation, something specifically designed to meet the needs of an emergency situation.

In presenting evidence to the CSM working party on Adverse Reactions, a joint Committee from the Association of Anaesthetists of Great Britain and Ireland and the Faculty of Anaesthetists of the Royal College of Surgeons stated 'We ... feel that the present arrangements for reporting are not suitable for the acute situation such as exists in anaesthetic practice, obstetrics, intensive care and accident and emergency units (and possibly in the postoperative recovery rooms). In particular, the yellow form is unsuitable for the appropriate recording of an acute incident'. This view was again expressed at the recent Linkman Conference at the Annual General Meeting, which was attended by both the Chairman and Secretary of the Committee on Safety of Medicines. Furthermore, the joint working party of the Association and Faculty is designing a card suitable for use by anaesthetists—whether this is acceptable to the CSM remains to be seen.

Despite these problems, we have a duty to both our patients and the profession to improve reporting by anaesthetists. If anyone wants guidance as to what to report, this is clearly set out in the British National Formulary (pp. 25, 26 of current issue) ... report any suspected adverse drug reactions which are potentially dangerous, incapacitating or lethal: they should be reported even though the toxic effect is well recognised'. The BNF gives details of the available Freefone service and other useful information on reporting of side effects.

In recent accreditation visits to hospitals, the author has questioned many anaesthetists, at all levels of seniority, on their attitude to the yellow cards and reporting drug side effects. The answers were very variable and showed no predictable pattern. Many juniors, particularly those who had recently worked in medical wards, were keen on reporting, but some had difficulty in getting cards when needed; others asked advice from their seniors (including Senior Registrars) most of whom were unhelpful. In only about one third of hospitals were there cards available in the operating theatres and/or secretaries' office. In no instance was there any clear policy on reporting reactions, nor was there any routine reporting to the CSM of undesirable drug effects reported at 'morbidity meetings'. The impression was one of apathy and doubts as to the value of the whole exercise. This is not a worthy attitude of a specialty which claims to know more about drugs than many clinical pharmacologists. If our suggestions on reporting etc., are not taken seriously by the CSM, could this be, at least in part, due to our poor track record in this field?

Department of Anaesthetics,
Whitla Medical Building,
97, Lisburn Road,
Belfast, BT9 7BL.

J.W. DUNDEE

References

1. INMAN WHW, MUSHIN WW. Jaundice after repeated exposure to halothane: an analysis of reports to the Committee on Safety of Medicines. *British Medical Journal* 1974; **1:** 5–10.
2. CLARKE RSJ, DUNDEE JW, GARRETT RT, MCARDLE GK, SUTTON JA. Adverse reactions to intravenous anaesthetics. A survey of 100 reports. *British Journal of Anaesthesia* 1975; **47:** 575–85.

Anaesthesia, 1986, Volume 41, pages 351–352

Editorial

Adverse reactions to drugs and anaesthetists

The Committee on Safety of Medicines (CSM) is a government organisation in the United Kingdom similar to that of the Federal Drug Administration in the United States of America: the remits of both of these organisations include the overall safety of drugs. The CSM has a system of reporting of adverse reactions to any drugs by any doctor; this is based on confidential reports known as yellow cards.

Anaesthetists were the first specialty to receive a letter of warning from the CSM, based on yellow card reports. Dated 5 January 1974, this was titled 'Jaundice following repeat exposure to halothane'. It concluded that, 'The Committee recognise that widespread experience over many years has demonstrated the value of halothane as an anaesthetic. They have, however, encouraged the authors to publish their findings so that anaesthetists might be made aware of this additional evidence when assessing all the relative risks of the various anaesthetic agents in the clinical circumstances of each case.'

This warning letter was similar in its content to the report of Inman and Mushin published in the same week in the British Medical Journal.[1] This was primarily intended to guide anaesthetists in their choice of drugs for repeat anaesthetics, but subsequent correspondence to medical journals showed that it was not appreciated by the specialty, although a few anaesthetists clearly understood its message. In retrospect, one has to realise what a boon halothane had become to anaesthetists; it was easy to administer and allowed rapid change in depth of anaesthesia, trichloroethylene being the only widely used nonflammable alternative. There were some correspondents who saw this either as a form of dictatorship or who doubted the scientific value of the reports received. Clearly, many had not used this means of reporting adverse effects of drugs.

It may have been a coincidence, or evidence of a lack of confidence between anaesthetists and the drug regulatory authorities, but the next (and to date the largest) report of side effects of drugs was a joint venture by an academic department and a pharmaceutical company.[2] This highlighted the anaphylactoid response to intravenous anaesthetics, something of which we have become very aware since the loss of Althesin and Epontol. Of the 100 adverse reports analysed, only 17 had been reported to the CSM. Even then it was clear that there was gross underreporting of adverse reactions to the CSM by anaesthetists.

Side effects of drugs is a topical issue and receives much attention by the media. The most outstanding example is what has been referred to as the 'Opren scandal': an alleged delay in the removal of a nonsteroidal anti-inflammatory drug from clinical use was blamed by some for deaths, particularly in the elderly.

While side effects of anaesthetic drugs are frequently described in the anaesthetic journals, why is there this low reporting to the official channels? Anaesthetists, who actually *give* more drugs than any other physician, have some specific problems in reporting side effects, which do not apply to the same extent to other specialties, although they apply to those working in intensive therapy units or casualty departments. There can be difficulty in recognising an abnormal reaction and appreciating its significance. No other specialty sees as much hypotension or apnoea without alarm and to distinguish between the normal and abnormal is not always easy. There is the problem of motivation to report any incident—why bother?—it will make no difference! Others may leave this to the academics or to their juniors. A small minority may have problems of honesty in assessing the situation and resulting troublesome thoughts on possible medicolegal implications. However, they can be assured of the confidentiality of the reports sent to the CSM.

More important are the logistic problems of completing the yellow cards. Many anaesthetists work single-handedly, some have multiple sites of work, with morning and afternoon sessions in different

0003–2409/86/040351 + 02 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

hospitals or different theatres in the same hospital. The heavy work schedule of some does not allow time to complete records between cases, without disruption of the operating session. This contrasts with the more leisurely work schedule of most physicians or family practitioners, who contribute the majority of reports. These usually have ready access to secretarial help and most have offices, while there are anaesthetists who are fortunate even to have a locker.

Nor are the existing yellow cards themselves free from problems. Firstly, there are the practical problems of where to store them, so as to be immediately available when required. Theatre sisters and hospital pharmacists could play a useful part here, but some do not appear to be willing to cooperate (or perhaps they have not had the problem explained properly).

Finally, there is a pressing question: is the yellow card, as at present designed, suitable for use in an emergency? Most anaesthetists would agree that they need something more relevant to their situation, something specifically designed to meet the needs of an emergency situation.

In presenting evidence to the CSM working party on Adverse Reactions, a joint Committee from the Association of Anaesthetists of Great Britain and Ireland and the Faculty of Anaesthetists of the Royal College of Surgeons stated 'We ... feel that the present arrangements for reporting are not suitable for the acute situation such as exists in anaesthetic practice, obstetrics, intensive care and accident and emergency units (and possibly in the postoperative recovery rooms). In particular, the yellow form is unsuitable for the appropriate recording of an acute incident'. This view was again expressed at the recent Linkman Conference at the Annual General Meeting, which was attended by both the Chairman and Secretary of the Committee on Safety of Medicines. Furthermore, the joint working party of the Association and Faculty is designing a card suitable for use by anaesthetists—whether this is acceptable to the CSM remains to be seen.

Despite these problems, we have a duty to both our patients and the profession to improve reporting by anaesthetists. If anyone wants guidance as to what to report, this is clearly set out in the British National Formulary (pp. 25, 26 of current issue) ... report any suspected adverse drug reactions which are potentially dangerous, incapacitating or lethal: they should be reported even though the toxic effect is well recognised'. The BNF gives details of the available Freefone service and other useful information on reporting of side effects.

In recent accreditation visits to hospitals, the author has questioned many anaesthetists, at all levels of seniority, on their attitude to the yellow cards and reporting drug side effects. The answers were very variable and showed no predictable pattern. Many juniors, particularly those who had recently worked in medical wards, were keen on reporting, but some had difficulty in getting cards when needed; others asked advice from their seniors (including Senior Registrars) most of whom were unhelpful. In only about one third of hospitals were there cards available in the operating theatres and/or secretaries' office. In no instance was there any clear policy on reporting reactions, nor was there any routine reporting to the CSM of undesirable drug effects reported at 'morbidity meetings'. The impression was one of apathy and doubts as to the value of the whole exercise. This is not a worthy attitude of a specialty which claims to know more about drugs than many clinical pharmacologists. If our suggestions on reporting etc., are not taken seriously by the CSM, could this be, at least in part, due to our poor track record in this field?

Department of Anaesthetics,
Whitla Medical Building,
97, Lisburn Road,
Belfast, BT9 7BL.

J.W. DUNDEE

References

1. INMAN WHW, MUSHIN WW. Jaundice after repeated exposure to halothane: an analysis of reports to the Committee on Safety of Medicines. *British Medical Journal* 1974; **1:** 5–10.
2. CLARKE RSJ, DUNDEE JW, GARRETT RT, MCARDLE GK, SUTTON JA. Adverse reactions to intravenous anaesthetics. A survey of 100 reports. *British Journal of Anaesthesia* 1975; **47:** 575–85.

Editorial notices

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1**: 532–5). Details will be found in the Notice to contributors to *Anaesthesia* at the end of this issue.

News and Notices sections

The first issue of each quarter will contain full News and Notices sections.

Copy dates for these will be: 13 June 1986 for September 1986, 12 September 1986 for January 1987 and 12 December 1986 for April 1987.

Supplementary News and Notices sections will be published in other issues but they will contain only material which requires publication before the next full News and Notices section.

Anaesthesia, 1986, Volume 41, 354–357

Vecuronium induced neuromuscular blockade

The effect of increasing dose on speed of onset

W. R. CASSON AND R. M. JONES

Summary

The speed of onset of neuromuscular blockade was measured for increasing doses of vecuronium. Onset times were found to be shorter with larger doses, up to a limit of $ED_{95} \times 3$ *(0.15 mg/kg). Thereafter, increasing the dose, even up to* $ED_{95} \times 8$ *(0.4 mg/kg), did not appreciably shorten the time to full neuromuscular blockade. The clinical implications of, and pharmacokinetic basis for, these findings are discussed.*

Key words

Neuromuscular relaxants; vecuronium.

Vecuronium, even in large doses, has a low propensity to initiate histamine release and a lack of cardiovascular side effects.[1] We have studied speed of onset of neuromuscular blockade using increasing doses of the drug.

Methods

After local ethics committee approval and with informed consent, we studied 25 ASA classes 1 or 2 patients undergoing surgery which required muscle relaxation. No patient greater than 20 percent above ideal body weight was included in the study. They were allocated to receive vecuronium in a dose of ED_{95} (0.05 mg/kg), × 2, × 3, × 4, or × 8 depending on the anticipated duration of surgery.

Prior to induction of anaesthesia, the left arm was immobilised in a standardised manner using a splint, and the left thumb was attached to a miniature force transducer, in order to measure isometric contractions of the adductor pollicis.[2] The strength of contraction was recorded using a Devices pre-amplifier and two-channel chart recorder. A 23-gauge indwelling needle was inserted in a vein on the dorsum of the right hand and thiopentone in a dose 20 percent greater than that required to abolish the eyelash reflex was administered and flushed in with normal saline. Stimulation of the left ulnar nerve was by supramaximal 0.2 ms square wave impulses delivered in a train-of-four pattern at 2 Hz for 2 s via surface electrodes at the wrist, repeated at 12-second intervals (Myotest). Immediately following a control train, vecuronium in the chosen dose was injected through the indwelling needle and flushed in with normal saline. The patients' lungs were ventilated with 50 percent nitrous oxide in oxygen, supplemented with 1 percent halothane and the trachea was in-

---

W.R. Casson, FFARCS, Lecturer, R.M. Jones, FFARCS, Senior Lecturer, Department of Anaesthetics, The United Medical and Dental Schools of Guy's and St Thomas's Hospitals, London Bridge, London SE1 9RT.
Correspondence should be addressed to Dr R.M. Jones please.

The results of this study were reported to the Anaesthetic Research Society in Leicester in March 1985.

0003–2409/86/040354 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Age, weight and sex characteristics

	Vecuronium dose (mg/kg)				
	0.05	0.10	0.15	0.20	0.40
(ED_{95} X)	(1)	(2)	(3)	(4)	(8)
n	5	5	5	5	5
Male	0	3	3	2	4
Female	5	2	2	3	1
Mean, age, years, (SD)	37 (14)	34 (14)	44 (25)	47 (14)	48 (25)
Mean weight, kg (SD)	69 (7)	72 (15)	68 (13)	69 (9)	61 (11)

tubated 3 minutes after injection of the relaxant or when there was no recordable first twitch. Ventilation was via a Bain co-axial breathing system with a fresh gas flow designed to maintain normocarbia. After intubation, the concentration of halothane was reduced to 0.5 percent and that of nitrous oxide increased to 66 percent.

The time from vecuronium injection to the first depression of the response of the first twitch (T1) to ulnar nerve stimulation (latent onset time) and the time from then to depression of T1 to 5 percent or less of control (manifest onset time) were recorded. Total onset time was derived by addition of latent and manifest onset times.

Results

Data are expressed as mean (SD) where applicable. The age, weight and sex characteristics are shown in Table 1. The groups who received the larger doses tended to be older because these patients underwent lengthy surgery and were therefore deemed suitable to receive a sizeable bolus of relaxant at induction.

Latent onset times are shown in Table 2. Manifest onset times are shown in Table 3. Total onset times are plotted in Fig. 1. Increasing the dose of vecuronium, up to $ED_{95} \times 3$ (0.15 mg/kg), was associated with a statistically significant (Students' *t*-test) decrease in total onset times; larger doses than this were not associated with any appreciable increase in the speed of onset. The reduction in onset time was achieved by reductions in both latent and manifest components.

Table 2. Latent onset times of neuromuscular blockade with increasing doses of vecuronium

	n	Time seconds, (SD)
Dose (mg/kg)		
0.05	5	82 (4.5)
0.10	5	74 (19.0)
0.15	5	53 (21.0)
0.20	5	44 (14.0)
0.40	5	43 (11.0)

Table 3. Manifest onset times of neuromuscular blockade with increasing doses of vecuronium

	n	Time seconds (SD)
Dose (mg/kg)		
0.05	5	109 (28.0)
0.10	5	85 (27.0)
0.15	5	46 (7.0)
0.20	5	51 (20.0)
0.40	5	44 (15.0)

Discussion

The disadvantages of suxamethonium, particularly its influence on cardiac rate and rhythm as well as intra-ocular and intragastric pressures, have led to the search for an alternative drug or technique to provide rapid neuromuscular blockade. The attainment of swift muscle relaxation is particularly important during the rapid sequence induction of anaesthesia in the patient with a full stomach. An ideal solution to this problem would be a nondepolarising relaxant with an onset time similar to that of suxamethonium. However, when given in standard clinical doses, competitive relaxants do not have sufficiently short onset times.

One approach to the acceleration of neuromuscular blockade has been to 'prime' patients with a small dose of nondepolarising relaxant prior to injection of the main dose.[3] However, using this technique, some patients have experienced significant subjective weakness necessitating early induction of anaesthesia.[4] The intro-

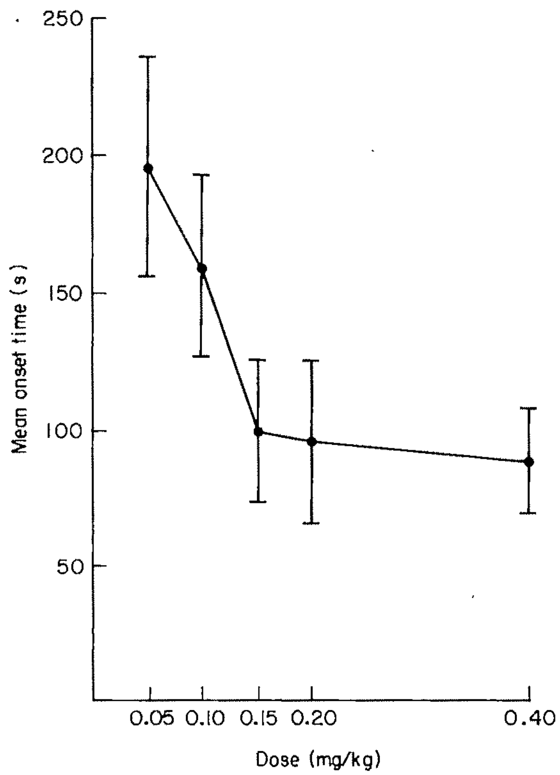


Fig. 1. Total onset times of neuromuscular blockade.

duction of vecuronium, with its low propensity to initiate histamine release and lack of cardiovascular side effects,[1] has raised the possibility of using very large doses in an attempt to accelerate the onset of action. The shorter duration of action of this agent, compared to other nondepolarising relaxants, is also a useful property if very large doses are to be administered during the induction sequence, in order to minimise the onset time.

Onset of neuromuscular blockade is a complex interaction of pharmacokinetic and pharmacodynamic factors.[5,6]. Intravenous injection leads to the rapid attainment of peak plasma levels, which then decline exponentially as redistribution occurs (alpha phase); it is during this period that the onset of drug action occurs. The magnitude of the lag between peak plasma levels and initial drug effect depends on a number of variables. On the assumption that drug diffusion and receptor occupancy are instantaneous, the most important of these factors are muscle blood flow and the blood–tissue partition coefficient.[7] With higher drug dosages, both the initially more rapid decline in plasma levels and sigmoid relation of these levels to drug effect, might lead one to anticipate a plateau effect, whereby increasing the dose above a certain level would lead to only a marginal increase in speed of onset. This study has conclusively demonstrated that this limit does indeed occur for vecuronium at a dose of 0.15 mg/kg (ED_{95} × 3). Both latent and manifest onset times depend on the complex relationship between plasma level and drug effect. It appears that a reduction in both these components contributes to the reduction in total onset time as the dose is increased to ED_{95} × 3.

Clearance of vecuronium from the plasma depends on both redistribution and elimination. The latter is mainly via hepatic uptake and biliary excretion, although 20–30 percent is excreted in the urine and 5 percent is metabolised to 3–OH vecuronium.[8] With increasing dose, elimination becomes the principal mechanism terminating drug effect as the volume of distribution becomes saturated. Therefore, not only does it serve no purpose, in terms of onset time, and time to intubation, to use a dose greater than $ED_{95} \times 3$, but this may lead to greatly prolonged neuromuscular blockade. Our anticipation of this problem led us to administer the largest doses of vecuronium only to those patients who were to undergo prolonged procedures, or who were to be electively ventilated postoperatively.

Suxamethonium provides good conditions for tracheal intubation within 60 seconds of intravenous administration.[9] It is well known that complete loss of muscle twitch in adductor pollicis may precede complete loss of muscle power in the diaphragm and the musculature of the pharynx and larynx. Therefore, if intubation were to be attempted after our minimum mean total onset time of 87 seconds, there could be no guarantee that the conditions would be as favourable as after suxamethonium administration.

In conclusion, we have demonstrated that the onset of vecuronium-induced neuromuscular blockade is hastened by administering an increasing dose of the drug, up to 0.15 mg/kg ($ED_{95} \times 3$). Doses in excess of this do not appreciably shorten onset time. This reduction with increasing dose is due to a reduction in both the latent and the manifest components of total onset time. Although this study was not designed to compare intubating conditions, our results suggest that even using the optimal dose for rapid onset, vecuronium does not provide intubating conditions comparable to those following suxamethonium 60 seconds after administration. However, similar conditions should prevail between 90 and 120 seconds after the administration of an $ED_{95} \times 3$ dose of vecuronium, and this may be considered as an alternative to suxamethonium if the latter drug is specifically contraindicated.

References

1. Marshall IG, Agoston S, Booij LHDJ, Durant NN, Foldes FF. Pharmacology of Org NC45 compared with other non-depolarizing neuromuscular blocking drugs. *British Journal of Anaesthesia* 1980; **52**: 11–9S.
2. Stanec A, Stanec G. The adductor pollicis monitor—apparatus and method for the quantitative measurement of the isometric contraction of the adductor pollicis muscle. *Anesthesia and Analgesia* 1983; **62**: 602–5.
3. Foldes FF, Schwarz S, Ilias W, Lackner F, Nagashima H, Mayrhofer O. Rapid tracheal intubation with vecuronium: the priming principle. *Anesthesiology* 1984; **61**: A294.
4. Clarke RSJ, Gibson FM, Mirakhur RK, Lavery CG. The effect of 'priming' on intubating conditions after vecuronium: a pilot study. *British Journal of Anaesthesia* 1985; **57**: (abstract in press).
5. Miller RD. Pharmacokinetics of competitive muscle relaxants. *British Journal of Anaesthesia* 1982; **54**: 161–7.
6. Hull CJ. Pharmacodynamics of non-depolarizing neuromuscular blocking agents. *British Journal of Anaesthesia* 1982; **54**: 169–82.
7. Stanski DR, Sheiner LB. Pharmacokinetics and dynamics of muscle relaxants. *Anesthesiology* 1979; **51**: 103–5.
8. Bencini A, Scaf AHJ, Sohn YJ, Kersten V, Agoston S. Clinical pharmacokinetics of vecuronium. In: Agoston A, Bowman WC, Miller RD, Viby-Mogensen J, Eds. *Clinical experiences with Norcuron* 1983; 115–23. Amsterdam: Excerpta Medica.
9. Calvey TN, Williams NE. Drugs that act on the neuromuscular junction. In: *Principles and practice of pharmacology for anaesthetists* 1982: 159–86. Oxford: Blackwell Scientific Publications.

Anaesthesia, 1986, Volume 41, pages 358–362

A pre-induction test dose for suxamethonium

J. CARNIE

Summary

A two-part experimental and clinical study was conducted to determine the effects of administration of a pre-induction dose of suxamethonium, and to see whether the symptoms produced could form the basis of a test dose, to determine sensitivity to suxamethonium prior to administration of a full intubation dose. Suxamethonium was shown to produce distinctive clinical features characterised by signs of both extra-ocular muscle contraction and paresis, manifest by symptoms of eye and eyelid heaviness without generalised paresis. The dose response was determined in individuals with normal plasma cholinesterase, to a test dose of suxamethonium chloride of between 20 and 1 μg/kg. Individuals with abnormal plasma cholinesterase were shown to exhibit sensitivity to these low doses and were easily distinguished from those with normal enzyme.

A protocol is suggested which can conveniently establish, prior to induction, those individuals with a reduced ability to hydrolyse suxamethonium.

Key words

Neuromuscular relaxants; suxamethonium.

Prolonged paralysis is a well recognised problem associated with the use of suxamethonium. This is attributable to markedly reduced hydrolysis by plasma cholinesterase.[1] The initial neuromuscular effects of suxamethonium do not differ in individuals with abnormal cholinesterase and the duration of its action is dose related.[2]

Laboratory estimation of plasma cholinesterase and genotyping is not performed as a routine, is not available in many hospitals and would be impractical in many emergency situations. Non-depolarising muscle relaxants do not present the same genetically determined problem,[3] but test doses have been suggested to determine individual sensitivity.[4] The special sensitivity of the extra-ocular muscles was the basis of this test. Suxamethonium administration results in a profound systemic paralysis of rapid onset, associated with an initial widespread depolarisation manifest as muscle fasciculations.[5] Suxamethonium is also known to have a paretic and relaxant effect on the two muscle fibre types found in the extra-ocular muscles.[6]

The effects of small doses of suxamethonium given prior to induction of anaesthesia to determine an individual's sensitivity have not previously been investigated. The nature and effects of a test dose of suxamethonium were therefore investigated in volunteers and under clinical circumstances.

J. Carnie, FFARCS, Consultant Anaesthetist, Department of Anaesthetics, East Birmingham Hospital, Bordesley Green East, Birmingham.

0003–2409/86/040358 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Method

Ethical Committee permission was obtained for the volunteer and clinical study.

Twelve informed and consenting volunteers (anaesthetists) were given intravenous doses of suxamethonium of 20, 10, 5, 2, and 1 μg/kg. A skilled orthoptist measured changes in oculomotor tone using the standard, hand-held, optical device known as the Maddox Wing. Clinical tests of accommodation and visual acuity were also performed. The volunteers reported the symptoms they experienced after injection. They were positioned supine and semi-erect, with continuous monitoring of heart rate.

A group of 168 patients who were to receive suxamethonium 1 mg/kg in the course of routine anaesthesia for a wide variety of surgical procedures formed the clinical group. They also were given a pre-induction dose of suxamethonium, either 20, 10, 5, or 2 μg/kg. Those who had no documented record of prior uneventful administration of suxamethonium were given an initial 1 μg/kg dose. This group of patients were asked to report the occurrence of any symptoms they experienced and, only if this was negative, were they asked any direct questions. They were positioned supine and were given the test drug via an indwelling venous cannula. Heart rate was monitored throughout. At 1 and 2 minutes after the injection of the drug, they were asked to perform a sustained head lift.

The duration of action of the intubation dose of suxamethonium (1 mg/kg) was followed by train-of-four stimulation of the ulnar nerve at the wrist, as well as observation of the return of the resultant thumb adduction. All of the volunteers and those patients with a prolonged response to the intubation dose of suxamethonium had cholinesterase estimation and genotyping performed on blood taken after completion of their clinical observations.

Results

After administration of the 20 μg/kg dose, ten of the 12 volunteers reported the onset of a sensation of heaviness localised to the eyes and eyelids, together with the sensation of an initial involuntary movement of the eyes. Six of these subjects experienced a transient blurring of vision, although no formal defect of accommodation or visual acuity could be demonstrated.

Table 1. Test solution preparation

μg/kg	mg suxamethonium added to 500 ml normal saline	ml injectate given per 10 kg body weight
20	500	0.2
10	250	0.2
5	125	0.2
2	50	0.2
1	25	0.2
1000	Standard preparation 50 mg/ml (Duncan Flockhart)	0.2

Table 2. Ocular test group details

	Mean (range)	
Age (years)	31.0	(25–40)
Weight (kg)	78.8	(60–98)
Sex	12 M	0 F

Table 3. Clinical study group details

	Mean (Range)	
Age (years)	37.1	(16– 80)
Body weight (kg)	62.0	(32–102)
Sex	129 F	39 M

Table 4. Maddox Wing test details

Subjects genotype $n = 10$	E_1^u, mean	E_1^u (SD)
Time of maximum defect (seconds) $n = 9$	58.6	(28.0)
Duration dioptre changes (seconds) $n = 9$	96.6	(25.0)
Duration of ocular symptoms (seconds) $n = 8$	154.0	(25.0)

Table 5. Incidence of ocular symptoms and measured defects following suxamethonium

μg/kg	n	Symptoms	Maddox Wing changes
20	12	10	11
10	10	6	5
5	10	3	2
2	10	1	0
1	10	0	0

All subjects had a full range of ocular movement, but it was described as sluggish. The majority reported that a voluntary effort was required to

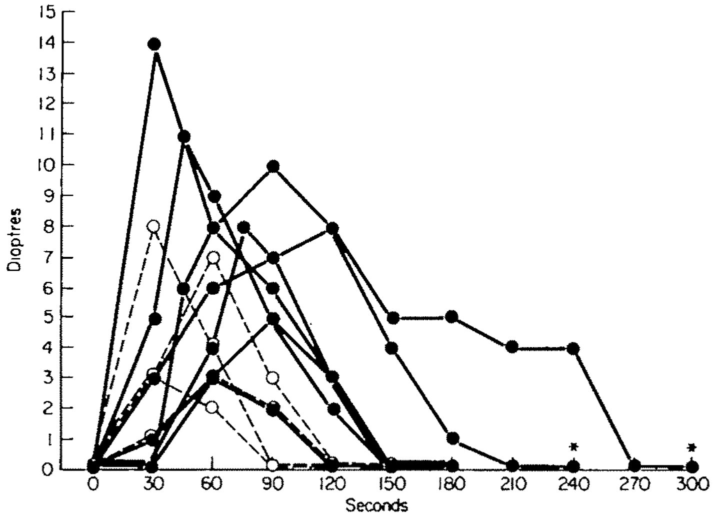


Fig. 1. Measured Maddox Wing horizontal plane readings, given as change from control values, at the 20 μg/kg suxamethonium dose. (●), Convergent response; (○), divergent response; (★), heterozygote.

maintain their eyes fully open. No enophthalmos was clinically observed.

Eleven subjects had changes in the Maddox Wing readings. Divergence occurred in seven subjects with an initial normal Maddox Wing reading. Convergence occurred in four who showed an initial moderate exophoria. In all subjects, movement was confined to the horizontal plane. Table 4 details the Maddox Wing changes in subjects who were subsequently shown to have normal plasma cholinesterase. Figure 1 details the dioptre changes measured by the Maddox Wing test for the 11 subjects who experienced changes from their control readings.

Two individuals demonstrated marked sensitivity at the 20-μg test dose. They reported persistent sensations of ocular heaviness (210 seconds, 270 seconds) and longer durations of abnormal Maddox Wing readings (180 seconds, 240 seconds). An exaggerated dioptre change was not noted in either individual. One was later shown to have the genotype E_1^u, E_1^u, and the other E_1^u, E_1^f.

Repeated administration of 10, 5, 2, 1 μg/kg doses was carried out to determine the symptomatic responses at these dosage levels. Table 5 details the incidence of reported ocular symptoms. The two individuals who were asymptomatic at the highest test dosage were not tested further.

At the 5-μg dose of suxamethonium, it was noted that the symptoms and measured ocular changes were similar to those reported at the highest test dose only in the two heterozygotes. At this dosage, one individual with normal enzyme reported the sensation of minimal and indistinct heaviness of a short duration. One of the heterozygotes reported symptoms of a barely discernible sensation of heaviness at the 2-μg dose, but no ocular defect could be demonstrated with repeated testing. The 168 patients who consented to the administration of a test dose of suxamethonium were given one of the four test dosages, with 122 patients receiving an initial 1 μg/kg. At this dose everyone remained asymptomatic, including three individuals who were subsequently shown to be heterozygotes for abnormal cholinesterase.

Four groups were chosen to establish dose responses to suxamethonium. The largest group of 75 individuals established the distinctive nature of the ocular symptoms, and showed the ease with which symptoms were reported by the test subjects. As in the experimental study, identical symptoms of heaviness of the eyes were reported, of the same distinctive nature as in the volunteer study, i.e. symptoms of heaviness of the eyelids and eyes, with sluggish eye movement. A minority reported slight transient blurring of vision and sensations of pressure on the globes.

Table 6. Details of individuals with normal duration of paralysis after suxamethonium chloride 1 mg/kg

Pre-induction suxamethonium μg/kg	*n*	Ocular symptoms reported	Duration symptoms mean (SD) (minutes)	Duration of full paralysis mean (SD) (minutes)
20	74	70 (95%)	2.2 (0.4)	4.7 (1.5)
10	30	15 (50%)	1.7 (0.3)	4.1 (1.5)
5	30	4 (13%)	1.5 (1.5)	3.8 (1.4)
2	30	0 (0%)	— —	4.5 (1.6)

Table 7. Details of individuals with abnormal duration of paralysis after suxamethonium chloride 1 mg/kg

Pre-induction suxamethonium, μg/kg	*n*	Duration ocular symptoms (minutes)	Duration of full paralysis (minutes)	Enzyme genotype
20	1	6	14	E_1^u E_1^a
10	1	4	12.5	E_1^u E_1^a
5	1	3	15	E_1^u E_1^a
2	1	0	10	E_1^u E_1^a

At the largest test dose, bilateral ptosis was frequently observed. Symptoms were freely reported and the majority did not require direct questioning to elicit symptoms. Onset and cessation of the ocular symptoms appeared well defined by all patients. No discomfort or untoward effects were observed or reported. Three individuals reported prolonged ocular symptoms and were subsequently shown to be heterozygotes for atypical cholinesterase. The individuals with a normal response after intubation with the drug reported indistinct and transient ocular symptoms at the 5-μg dosage, in contrast to the heterozygote who reported symptoms similar to the distinctive features seen with the highest dosage. All the 30 patients given 2 μg/kg of suxamethonium remained asymptomatic; one of these was observed to have a prolonged complete paralysis period after her intubation dose. She was shown to be a heterozygote for abnormal cholinesterase. Table 6 details the incidence and characteristics of the test doses in individuals with a normal response to suxamethonium, as indicated by a duration of full paralysis not exceeding 10 minutes. Table 7 details the four individuals found to be heterozygote for atypical cholinesterase. At all of the test doses given, of 20, 10 and 5 μg/kg, no individual who was asymptomatic, or who reported symptoms for less than 3 minutes, had a paralysis for longer than 10 minutes after 1 mg/kg of the drug, other than the heterozygote in the group given the 5-μg dosage.

Premedication with temazepam 20 mg, 1–2 hours pre-operatively was found not to interfere with the reporting of ocular symptoms, since there was a similar incidence of reported symptoms from the 33 unpremedicated and the 135 premedicated patients.

Full unsupported head control was maintained in all subjects and no symptoms attributable to any generalised paretic effect were reported. No significant changes in heart rate or rhythm occurred with the test dose or the subsequent intubation dosage.

Discussion

Suxamethonium administered in a dose of 20 μg/kg to individuals with a normal response to an intubation dose of 1 mg/kg produces clear and distinctive ocular symptoms without systemic paresis. These symptoms are also produced at the reduced dosage of 5 μg/kg in individuals heterozygous for abnormal plasma cholinesterase. A minority of normal individuals remained asymptomatic at the largest test dose; this is attributable to circulatory delay[7] with complete metabolism or possibly to the presence of the C5 variant associated with rapid hydrolysis of suxamethonium.[8]

The symptoms associated with the test dose are due to the net contraction of the multiply innervated extra-ocular muscle fibres, combined with relaxation of the singly innervated muscle fibres. This produces movement of the eye towards the muscle with the greatest reduction in length. These ocular effects occur together with a change in oculomotor tone which is considerably less than the dipotre change noted after small precurarising doses of non-depolarising muscle relaxants.[4] The symptoms produced by suxamethonium are as distinctive, but differ as a result of their rapidity of onset, active contraction component and short duration.

In this study, individuals with normal enzyme exhibited clear symptoms at one fiftieth of the intubation dose of suxamethonium employed, whereas heterozygote individuals only required one two-hundredth of this intubation dose. Homozygotes have been shown to be paralysed for periods of 10–30 minutes by doses of suxamethonium of 1–10 mg.[9–11] As these individuals would metabolise none of an injected dose of suxamethonium, the 2 μg/kg dose would form a suitable test concentration to administer initially, to determine an individual's sensitivity to suxamethonium. This solution would not cause any symptoms in the majority of patients and could then be given at 2.5 times its initial volume (equal to 5 μg/kg) to determine whether an individual responded as a heterozygote for atypical cholinesterase.

The incidence (1:41) of heterozygote individuals found in the population of this study is in close agreement with that of another British study;[12] both studies chose duration of action as the important measure of suxamethonium sensitivity. The true incidence of the heterozygote genotype,[1] at 1:28, does not allow for the overlap between the activities found in normal individuals and heterozygotes.[13]

Chairside dentistry and electroconvulsive therapy are often performed in circumstances where delayed onset of spontaneous respiration after suxamethonium administration are particularly unsuited to coping with prolonged ventilation. This test could be used to particular advantage in these circumstances. By adopting this test procedure, an anaesthetist can, within a few minutes, pre-operatively determine an individual's ability to metabolise suxamethonium and would therefore be able to modify his choice of relaxant and thus prevent any major problems associated with the use of this agent.

References

1. Feldman S. Neuromuscular blocking drugs. In: Churchill-Davidson, H.C., ed. *A practice of anaesthesia*, 4th edn. London: Lloyd-Luke, 1979: 868.
2. Walts LF, Dillon JB. Clinical studies on succinylcholine chloride. *Anesthesiology* 1967; **28:** 372–6.
3. Kalow W. Pharmacogenetics and anesthesia. *Anesthesiology* 1964; **25:** 377–87.
4. Hanington-Kiff JG. Residual post-operative paralysis. *Proceedings of the Royal Society of Medicine* 1970; **63:** 73–6.
5. Durant NN, Katz RL. Suxamethonium. *British Journal of Anaesthesia* 1982; **54:** 195–208.
6. Dillon JB, Sabawala P, Taylor DB, Gunter R. Action of succinylcholine on extraocular muscles and intraocular pressure. *Anesthesiology* 1957; **18:** 44–53.
7. Harrison GA, Junius F. The effect of circulation time on the neuromuscular action of suxamethonium. *Anaesthesia and Intensive Care* 1972; **1:** 33–40.
8. Harris H, Hopkinson DA, Robson EB, Whittaker M. Genetical studies on a new variant of serum cholinesterase detected by electrophoresis. *Annals of Human Genetics* 1963; **26:** 359–82.
9. Viby-Mogensen J. Succinylcholine neuromuscular blockade in subjects homozygous for atypical plasma cholinesterase. *Anesthesiology* 1982; **55:** 429–34.
10. Baraka A. Suxamethonium—neostigmine interaction in patients with normal or atypical cholinesterase. *British Journal of Anaesthesia* 1977; **49:** 479–84.
11. Kalow W. The distribution, destruction and elimination of muscle relaxants. *Anesthesiology* 1959; **20:** 505–18.
12. Owen H, Hunter AR. Heterozygotes for atypical cholinesterase. *British Journal of Anaesthesia* 1983; **55:** 315–8.
13. Viby-Mogensen J. Succinylcholine neuromuscular blockade in subjects heterozygote for abnormal plasma cholinesterase. *Anesthesiology* 1981; **55:** 231–5.

Anaesthesia, 1986, Volume 41, pages 363–369

An investigation of factors affecting postoperative rewarming of adult patients

F. CARLI, M. GABRIELCZYK, MARGARET M. CLARK AND V. R. ABER

Summary

Aural canal temperature was measured for one hour after arrival in the recovery room in 200 adult patients who underwent one of the following types of major surgery: abdominal, pelvic, vascular, orthopaedic or prostatic. One group of 100 patients was studied in the recovery room of Hammersmith Hospital which was not equipped with a controlled system for constant ventilation and humidification, while the other 100 patients were studied in the recovery room of Edgware General Hospital, which had a constant ambient temperature and controlled relative humidity with 20 air changes/hour. The rate of rewarming was found to be similar in both groups. Within the range of ambient temperatures and relative humidities measured, patients over 60 years of age rewarmed more slowly than did patients under 60 years ($p < 0.05$). *General anaesthesia was associated with significantly faster rewarming than was local anaesthesia* ($p < 0.01$).

Key words

Temperature; body, monitoring.
Hypothermia; postoperative.

Low environmental temperature, cold intravenous fluids, ventilation of the lungs with cold gases, exposure of body cavities, absence of muscle movements and drug induced vasodilatation all contribute to heat loss during anaesthesia. As a result, patients often arrive in recovery rooms with a low body temperature. During the early postoperative period, hypoxia can occur as a result of increased metabolic rate and oxygen demand,[1] so cooling and shivering should be prevented if possible. In homeotherms, heat conservation is usually very effective[2] and a thermoneutral environment[3] might play an important role in conserving body heat. Two groups of patients were therefore investigated during the rewarming period after surgery in two dissimilar recovery rooms, one with a controlled ambient temperature and humidity, the other without. In addition, other factors which may have contributed to the rate of rewarming were examined.

Methods

Two hundred patients admitted to the recovery rooms were studied, during the period from

---

F. Carli, FFARCS, Senior Registrar, Department of Anaesthetics, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0HS, M. Gabrielczyk, FFARCS, Registrar, Margaret M. Clark, FFARCS, Consultant, Department of Anaesthetics, Edgware General Hospital, Edgware, Middlesex, V. R. Aber, MSc, DIC, Senior Scientist, Department of Medical Physics, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0HS.

0003–2409/86/040363 + 07 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

January to May. One hundred patients were studied in Hammersmith Hospital and the remainder at Edgware General Hospital. The patients had undergone either intra-abdominal, pelvic, orthopaedic, peripheral vascular or prostatic surgery. Patients who were grossly obese or who had endocrine abnormalities or a pyrexia were not included. Informed consent was obtained in each case.

Premedication was with either papaveretum and hyoscine or pethidine and promethazine by intramuscular injection 90 minutes before surgery. General anaesthesia was induced with thiopentone and neuromuscular blockade established with either pancuronium or alcuronium. The lungs were ventilated to normocapnia with a mixture of nitrous oxide in oxygen, supplemented with either halothane, enflurane, fentanyl or phenoperidine. Local anaesthesia, when used, consisted of either lumbar subarachnoid or epidural block using either cinchocaine or bupivacaine; sedation was provided with an intravenous benzodiazepine. The height of the block was assessed by pin prick and recorded, aiming to establish anaesthesia to the level of the 11th thoracic dermatome.

The group of patients who underwent transurethral prostatic surgery at Edgware General Hospital had their bladder irrigated during and after the procedure with solutions warmed to 37.0°C. In Hammersmith Hospital, the solutions used were at room temperature. All intravenous fluids, except blood, were infused at room temperature and no active warming devices were used during surgery.

A thermocouple probe was inserted in the aural canal after induction of anaesthesia and temperature measurements were taken to estimate body core temperature before surgery, on admission to the recovery room and subsequently every 15 minutes for the first hour following surgery. All the probes and the thermometer were manufactured by Comark Electronics and were calibrated against a National Physical Laboratory mercury-in-glass total immersion thermometer in a stirred water bath. They were accurate to 0.05°C over the temperature range studied. The presence or absence of shivering was assessed by two of the authors (F. C. and M.G.).

The percentage of body fat in each patient in the Hammersmith Hospital group was determined by measuring skinfold thicknesses.[4]

Recovery rooms. Environmental characteristics

The main recovery room at the Hammersmith Hospital is a large area with four windows and seven radiators. It is not equipped with a controlled ventilation system and the daily ambient temperature and relative humidity therefore fluctuates according to the external environment. The air speed varies considerably as a result of draughts from the nearby operating theatres, stairs and lifts. The recovery room at Edgware General Hospital is part of the operating theatre suite and has a computerised system with controlled ventilation and humidification using 20 air changes/hour throughout the year. The five windows are sealed and the four radiators are only used in severely cold weather.

In the recovery rooms, ambient temperature was measured with a mercury-in-glass thermometer, relative humidity with a hair hygrometer (Negretti and Zambra) and air speed with a vane anemometer (Negretti and Zambra). All patients admitted to the recovery rooms were covered with one sheet and one blanket. The minimum stay in the recovery room was one hour, during which the body temperature was measured. Patients were transferred to the ward by the recovery room nurse, regardless of their body temperature measurements.

Statistical analysis. For each patient, the rewarming rate was calculated as the slope of the regression line of body core temperature on time (0, 15, 30, 45 and 60 minutes). This value was used as the dependent variable in the stepwise multiple regression analysis which determined the factors which were independently correlated with rewarming. Comparisons between two samples were done either by the two sample *t*-test, where distributions could be assumed to be approximately normal, or by the Mann-Whitney test, when the data were ordinal, or the Chi squared test for nominal data.

Results

The demographic details of the patients, the duration of surgery and the type of anaesthesia are shown in Table 1.

The two recovery rooms were significantly different in respect of ambient temperature and relative humidity. (Table 2) The air speed at Hammersmith Hospital was too unstable to be measured, while at Edgware General Hospital it

Table 1. Mean (range) group characteristics

	Hammersmith Hospital ($n = 100$) M = 46; F = 54	Edgware General Hospital ($n = 100$) M = 51; F = 49
Age (years)	57 (17–99)	61 (19–92)
Body weight (kg)	66.4 (37–100)	66.3 (43–98)
Height (cm)	167 (148–184)	170 (155–185)
Body fat (%)	32.6 (12–46)	Not measured
Duration of surgery (minutes)	103 (74–217)	121 (69–246)
Type of anaesthesia: General	79	85
Local	21	15

Table 2. Mean (range) recovery room environmental characteristics at respective hospitals

	Hammersmith Hospital	Edgware General Hospital
Recovery room temperature (°C)	22.4* (19–26)	22.9 (21–24)
Recovery room relative humidity (%)	47* (30–80)	55 (46–75)

*$p < 0.01$.

Table 3. Pre- and postoperative body temperatures and rate of rewarming of the respective groups. Mean (range)

	Hammersmith Hospital	Edgware General Hospital
Body temperature (°C):		
Before surgery	36.5 (35.3–37.6)	36.2 (35.0–37.0)
At admission to recovery	35.2 (32.8–36.7)	35.4 (33.5–36.6)
At discharge from recovery	35.6 (33.5–37.2)	35.9 (33.8–37.2)
Rate of rewarming (°C/hour)	0.52 (0.4–2.4)	0.56 (0.4–2.0)

Table 4. Admission and discharge body temperature for different operative procedures in the respective group Mean (range)

	Hammersmith Hospital			Edgware General Hospital		
Type of surgery	n	Admission body temperature (°C)	Discharge body temperature (°C)	n	Admission body temperature (°C)	Discharge body temperature (°C)
Intra-abdominal	41	35.2 (32.8–36.7)	35.8 (33.5–37.2)	43	35.2 (33.5–36.6)	35.8 (33.8–37.0)
Pelvic	23	35.3 (34.0–36.7)	35.9 (33.9–37.1)	21	35.7 (34.7–36.5)	36.4 (34.8–37.2)
Vascular or orthopaedic	16	35.1 (34.0–36.2)	35.4 (34.0–36.5)	13	35.3 (34.2–36.2)	35.9 (35.1–36.9)
Transurethral prostatic	20	35.2 (33.8–36.0)	35.3 (33.5–36.2)	23	35.2 (34.4–36.1)	35.5 (34.2–36.7)

was constant at a value of 0.24 m/second. Despite this, no difference was found between the body core temperatures of the two groups on recovery, admission or discharge from recovery rooms. The rate of rewarming was similar in both groups (Table 3). The results associated with different operative procedures are summarised i Table 4. No statistically significant difference wa found between the two hospitals in the body co temperatures measured on admission to the r covery rooms and prior to transfer to pos operative wards for different types of surgery.

Multiple regression analysis showed that age of the patient and type of anaesthesia were the most important factors affecting body temperature changes in the recovery room. The rate of rewarming following general anaesthesia was significantly different for patients under 60 years of age compared to those over 60 years ($p<0.05$, Fig. 1). In elderly patients, rewarming after local anaesthesia was significantly slower than in those who had general anaesthesia ($p<0.01$, Fig. 2). A similar rewarming pattern in the two age groups following local anaesthesia was found at Hammersmith Hospital (Fig. 3). Because of the small number of patients under 60 years of age receiving local anaesthesia, statistical significance could not be demonstrated. No patient under 60 years received local anaesthesia at Edgware General Hospital. Rewarming in elderly patients following prostatic surgery took place faster if they had general anaesthesia than if local anaesthesia had been administered; the values obtained were slightly higher at Edgware General Hospital (Fig. 4). No correlation was found between the rate of rewarming and either the length of surgery or percentage of body fat.

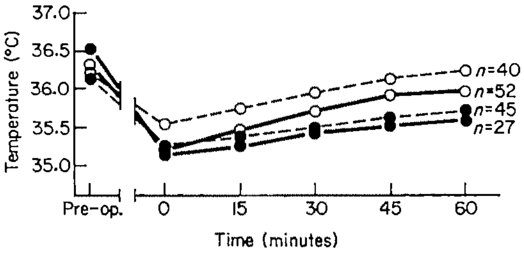


Fig. 1. Postoperative rate of rewarming of patients in two age groups who received general anaesthesia in the respective hospitals. ——, Hammersmith Hospital; ---, Edgware General Hospital; ●, >60 years; ○, <60 years.

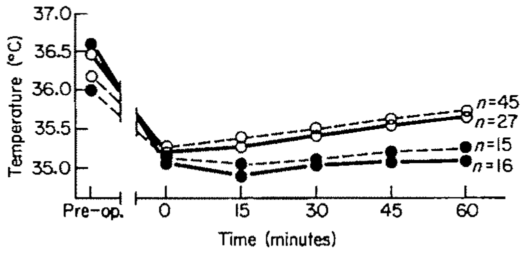


Fig. 2. Postoperative rate of rewarming of patients over 60 years of age who had general or local anaesthesia in the respective hospitals. ——, Hammersmith Hospital; ---, Edgware General Hospital; ●, local anaesthesia; ○, general anaesthesia.

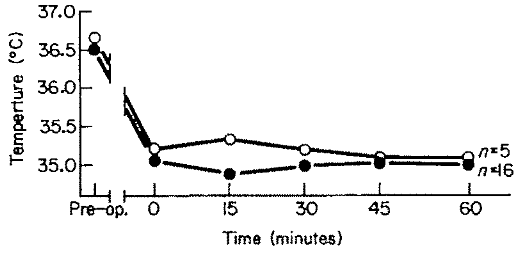


Fig. 3. Postoperative rate of rewarming of patients under 60 and over 60 years of age who received local anaesthesia at the Hammersmith Hospital. ●, >60 years; ○, <60 years.

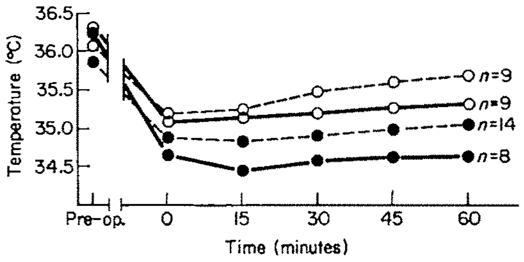


Fig. 4. Postoperative rate of rewarming of patients over 60 years of age who underwent transuretheral prostatic surgery, either under general or local anaesthesia in the respective hospitals. ——, Hammersmith Hospital; ---, Edgware General Hospital; ●, local anaesthesia; ○, general anaesthesia.

The incidence of shivering following general anaesthesia was 27 percent at Hammersmith Hospital and 25 percent at Edgware General Hospital, while that following local anaesthesia was 10 percent and 13 percent respectively. This difference was not statistically significant for either hospital. In patients under 60 years of age, the rewarming rate following general anaesthesia correlated with shivering, but did not do so in patients over 60 years.

Discussion

The results showed that the rate of rewarming in the recovery room during the first hour after surgery seemed unaffected by environmental characteristics. Whether this was controlled or not, the patients studied left the recovery rooms after one hour with body temperatures lower than their pre-operative values.

It is widely recognised that patients lose heat during surgery and are therefore hypothermic on arrival in the recovery room.[5] During recovery from anaesthesia, physiological mechanisms for maintaining body heat balance are re-established.[6] Although it is generally agreed that moderate hypothermia of brief duration is well tolerated by man, hypothermia may represent a significant clinical risk during the early postoperative period. The high metabolic rate during rewarming increases tissue oxygen demand by as much as 400–500 percent, which could be detrimental when cardiopulmonary reserve is impaired, especially in the elderly.[1,7] This results in increased cellular metabolism with lactic acid production. It has also been shown that increased protein degradation occurred postoperatively in elderly patients after major abdominal surgery, when no measures were taken to prevent perioperative and postoperative heat loss.[8,9]

Extensive studies have looked at environmental conditions in operating theatres and their effects on the body temperatures of surgical patients.[10] The majority of recovery rooms, being part of an operating theatre suite, have an average ambient temperature of 21°C and a relative humidity of 55 percent. The technical design data laid down by the Department of Health and Social Security in 1976[11] recommended an ambient temperature of 18°C for recovery rooms, but did not specify the relative humidity. The environment plays an important part in the thermal comfort of a surgical patient and depends on four variables: air temperature, relative humidity, air velocity and clothing resistance.[3] Several workers suggested that in order to provide adequate thermal comfort to a subject during sedentary activity, whose covering is a cotton blanket, the environment must have an ambient temperature of 25°C, relative humidity of 40 percent and an air speed of 0.05 m/second.[12]

Core temperature was measured by an auditory canal probe, chosen because it was well tolerated by the patient during the postoperative period. It was easily inserted and did not cause trauma as might happen with a tympanic membrane probe.[13] Provided care is taken at insertion to avoid draughts which might affect the reading, aural temperature correlates well with oesophageal temperature, as shown previously.[14] In addition, aural temperature is more reliable than shell cutaneous temperature, is non-invasive and is claimed to be a valid indicator of core temperature.[15,16] We did not measure mean skin temperature as this required the application of at least four probes at different sites on the body. Holdcroft and Hall[17] showed the importance of measuring core and mean skin temperature to explain the redistribution of heat occurring with different anaesthetic techniques. However, during the recovery period, the changes in both mean skin and core temperature reported by these authors following epidural and different types of general anaesthesia, were similar and comparable to those of the present study.[18]

When we consider the effect of age on the rate of postoperative rewarming, patients over 60 years of age receiving general anaesthesia showed a slower change compared with those under 60 years, and were discharged from the recovery room with an average body temperature of 35.5°C, 0.8°C lower than the pre-operative values. Although metabolism decreases with age,[19] Fanger[12] showed that elderly patients prefer the same thermal environment as young people. It is therefore the time taken to rewarm which is different in the two age groups and this could be ascribed to a reduced capacity in the elderly to raise their metabolic rate and a decreased pattern of vasomotor response to cold.[20]

The anaesthetic technique was the other significant factor which was found to influence rewarming in the recovery room. In the current study, the rate at which patients rewarmed following epidural or subarachnoid anaesthesia was significantly slower than that observed with general anaesthesia; these results were similar to those reported by Vaughan *et al.*[21] and Holdcroft *et al.*[18] It was interesting to find that patients over 60 and under 60 years of age had the same pattern of rewarming following local anaesthesia (Fig. 3). However, because the sample of under 60-year olds was too small, it was not possible to derive any significant conclusions on their postoperative rewarming rate. Local anaesthesia causes motor and sympathetic blockade, resulting in decreased shivering and peripheral vasodilatation; the extent of the latter is related to the height of the block. While local blocks have recognised beneficial effects on tissue oxygenation and intermediary metabolism,[22] it is not known whether prolonged hypothermia can be readily tolerated. It might be possible that the combination of heat preservation and local anaesthesia minimise the response to surgical stress. This aspect needs to be investigated further.

The patients who underwent transurethral prostatic surgery lost further heat during bladder irrigation. The small difference between Hammersmith Hospital and Edgware General Hospital might be due to the use of warmed irrigation fluids at the latter. However, the large difference between local anaesthesia and general anaesthesia was the most important factor in the rate of rewarming, as confirmed by other workers.[23,24]

No correlation was found between postoperative rewarming and either body fat or length of surgery. The incidence of shivering confirmed previous findings, which showed that a relationship between it and hypothermia remains controversial.[25–27] In the present study, 57 out of 72 elderly patients rewarmed without shivering, while 65 out of 92 under 60 years old shivered during rewarming. Postoperative rewarming following local anaesthesia could not be compared with those receiving general anaesthesia because of the small number of patients having local anaesthesia who shivered (4 out of 36). This observation contrasts with that of Holdcroft *et al.*,[8] who found a higher incidence of shivering following local anaesthesia, although they studied only female patients under 60 years of age receiving epidural analgesia to the T_8 level. The greater extent of vasodilatation found by the above authors and the age difference might explain their results.

In conclusion, the recovery room environment does not seem to affect postoperative rewarming. Perhaps much higher ambient temperatures and lower relative humidity may make a difference and this variable needs to be investigated. As the incidence of cardiorespiratory problems increases with age, it is mandatory to provide a space blanket and O_2 therapy to the elderly in our recovery rooms, since when their core temperature falls they are more vulnerable to the effects of hypoxia. Rewarming in patients over 60 years of age following local anaesthesia is slower than following general anaesthesia. Care must therefore be taken intra- and postoperatively, not to offset the advantages claimed from local anaesthesia by allowing body core temperature to fall unduly. Anaesthetists should be as aware of the importance and physiological implications of monitoring decreases in body temperature perioperatively as they are of detecting increases.

Acknowledgments

The authors are extremely grateful to the recovery room nurses of Hammersmith Hospital and Edgware General Hospital for their help and to Shirley Richens for typing the manuscript.

References

1. Bay J, Nunn JF, Prys-Roberts C. Factors influencing arterial Po_2 during recovery from anaesthesia. *British Journal of Anaesthesia* 1968; **40:** 398–406.
2. Hey EN. Thermal neutrality. *British Medical Bulletin* 1975; **31:** 69–74.
3. Monteith JL. Specification of the environment for thermal physiology. J.L. Monteith and L.E. Mount, eds. In: *Heat loss from animals and man.* London: Butterworth, 1974: 3–19.
4. Durnin JVGA, Womersley J. Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged 16 to 72 years. *British Journal of Nutrition* 1974; **32:** 77–97.
5. Vale JR. Normothermia, its place in operative and postoperative care. *Anaesthesia* 1973; **28:** 241–5.
6. Stephen CR. Postoperative temperature changes. *Anesthesiology* 1961; **22:** 795–9.
7. Roe CF, Goldberg MJ, Blair CS, Kinney JM. The influence of body temperature on early postoperative oxygen consumption. *Surgery* 1966; **60:** 85–92.
8. Carli F, Clark MM, Woollen JW. Investigation of the relationship between heat loss and nitrogen excretion in elderly patients undergoing major abdominal surgery under general anaesthetic. *British Journal of Anaesthesia* 1982; **54:** 1023–9.
9. Carli F, Itiaba K. Muscle proteolysis and body temperature changes associated with major abdominal surgery in elderly patients. *British Journal of Anaesthesia* 1985; **57:** 350–1P.
10. Morris RH, Wilkey BR. The effects of ambient temperature on patient temperature during surgery not involving body cavities. *Anesthesiology* 1970; **37:** 102–7.
11. Department of Health and Social Security. Engineering data; general issue 1976 Technical design data B2403, post-anaesthetic recovery.
12. Fanger PO. Assessment of man's thermal comfort in practice. *British Journal of Industrial Medicine* 1973; **30:** 313–24.
13. Wallace CT, Marks WE, Atkins WY, Mahaffey JE. Perforation of the tympanic membrane, a complication of tympanic thermometry during anesthesia. *Anesthesiology* 1974; **41:** 290–1.
14. Benzinger M. Tympanic thermometry in surgery and anesthesia. *Journal of the American Medical Association* 1969; **209:** 1207–11.
15. Vaughan MS, Cork RL, Vaughan RW. Inaccuracy of liquid crystal thermometry to identify core temperature trends in postoperative adults. Anesthesia and Analgesia 1982; **61:** 284–7.
16. Lees DE, Schuette W, Bull JM, Wang-Peng J, Atkinson ER, MacNamara TE. An evaluation of liquid-crystal thermometry as a screening device for intraoperative hyperthermia. *Anesthesia and Analgesia* 1978; **57:** 669–74.

17. Holdcroft A, Hall GM. Heat loss during anaesthesia. *British Journal of Anaesthesia* 1978; **50:** 157–64.
18. Holdcroft A, Hall GM, Cooper GM. Redistribution of body heat during anaesthesia. A comparison of halothane, fentanyl and epidural anaesthesia. *Anaesthesia* 1979; **34:** 758–64.
19. Emslie-Smith D. Hypothermia in the elderly. *British Journal of Hospital Medicine* 1981; **26:** 442–52.
20. Wagner JA, Robinson S, Marino RP. Age and temperature regulation of humans in neutral and cold environments. *Journal of Applied Physiology* 1974; **37:** 562–5.
21. Vaughan MS, Vaughan RW, Cork RC. Postoperative hypothermia in adults: relationship of age, anesthesia, and shivering to rewarming. *Anesthesia and Analgesia* 1981; **60:** 746–51.
22. Engquist A, Brandt MR, Fernandes A, Kehlet H. The blocking effect of epidural analgesia on the adrenocortical and hyperglycaemic responses to surgery. *Acta Anaesthesiologica Scandinavica* 1977; **21:** 330–5.
23. Allen TD. Body temperature changes during prostatic resection as related to the temperature of the irrigating solution. *Journal of Urology* 1973; **110:** 433–5.
24. Jenkins J, Fox J, Sharwood-Smith G. Changes in body heat during transvesical prostatectomy. A comparison of general and epidural anaesthesia. *Anaesthesia* 1983; **38:** 748–53.
25. Cohen M. An investigation into shivering following anaesthesia: preliminary report. *Proceeding of The Royal Society of Medicine* 1967; **60:** 752–3.
26. Jones HB, McLaren CAB. Postoperative shivering and hypoxaemia after halothane, nitrous oxide and oxygen anaesthesia. *British Journal of Anaesthesia* 1965; **37:** 35–41.
27. Pflug AE, Aasheim GM, Foster C, Martin RW. Prevention of post-anaesthesia shivering. *Canadian Anaesthetists' Society Journal* 1978; **25:** 43–9.

Anaesthesia, 1986, Volume 41, pages 370–374

Obstetric anaesthetic services in Scotland in 1982

D. B. SCOTT AND R. E. G. AITKEN

Summary

A recent survey of Scottish obstetric anaesthesia practice revealed that the majority of deliveries take place in the larger hospitals; these also have the highest epidural rates, both for relief of pain in labour and for Caesarean section. However, as epidural blockade is an essential part of modern obstetric practice, it is a matter of concern to achieve an equal standard in the medium-sized hospitals, whilst accepting that special arrangements are required in the very small obstetric hospitals.

Key words

Anaesthesia; obstetric.

In 1981 the Scottish National Medical Consultative Committee (NMCC) through its Anaesthetic Subcommittee collated information on the provision of obstetrical anaesthesia in Scotland, showing that the main problem appeared to be the large number of small, isolated maternity units requiring obstetrical anaesthetic services, many of which were at a considerable distance from a parent unit. As a result of this work, it was suggested that a multidisciplinary Working Group be set up to consider the subject. The NMCC established the Group in 1982, with the object of examining current standards of practice in obstetrical anaesthesia and analgesia in relation to maternal morbidity and mortality, and to make recommendations.

A small Working Group was set up, consisting of three anaesthetists, two obstetricians, two general practitioners and a midwife, with a consultant radiologist acting as Chairman, assisted by a Departmental medical officer and secretary. It was quickly decided that factual evidence was required regarding the present service and a questionnaire was prepared and sent to all hospitals undertaking obstetric care. The results of that survey form the basis of this paper.

Method

The questionnaire was designed to answer certain questions for the calendar year 1982, including: how many hospitals were involved in providing obstetric care and how many deliveries took place in each? How many patients required general anaesthesia? How many patients received epidural blockade, either for relief of pain in labour or for Caesarean section? Was there consultant participation in the service and what was the nature of that participation? What staff undertook emergency calls and how quickly could the duty anaesthetist be available? Were the arrangements for the obstetric anaesthetic service

---

D.B. Scott, MD, FRCPE, FFARCS, Consultant, Department of Anaesthetics, Royal Infirmary of Edinburgh, Lauriston Place, Edinburgh EM3 9YW, R.E.G. Aitken, MSc, MB, ChB, MFCM, Senior Medical Officer, Scottish Home and Health Department,

0003–2409/86/040370 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

considered satisfactory by the local anaesthetists? Were midwives instructed in the management of patients receiving epidural blockade? Would the anaesthetists welcome properly trained midwives being allowed to give epidural top-up doses? What help was available to the anaesthetist?

Results

Number of deliveries

All the hospitals circulated returned a completed questionnaire. The total number of deliveries performed according to the returns was 62 257, with three of the smaller general practitioner units not answering the question. The Registrar General's figures for registered births in 1982 was 66 582 (with 609 multiple births). Of these 65 901 births took place in National Health Service hospitals. Allowing for multiple births, the questionnaire total was therefore about 3000 fewer than the Registrar General's figures. There is therefore a probable 5% error in the questionnaire's factual data, but in such a survey, this is considered acceptable.

Hospitals

The hospitals were classified into four groups, depending upon the number of annual deliveries, as follows (Table 1): Group A, those with more than 2500 deliveries; Group B, those with 1500–2499 deliveries; Group C, those with 1000–1499 deliveries; Group D, those with less than 1000 deliveries.

There were 11 hospitals in Group A. In total, they delivered 37 579 mothers or 60.4% of the questionnaire's total. In Group B there were nine hospitals, which delivered 16 331 mothers or 26.2% of the total. In Group C there were four hospitals, which delivered 5290 mothers or 8.5% of the total. Group D varied from 37 to 567 deliveries. There were 17 hospitals in this category, with a total of 3057 deliveries (with three not recording the number) or 4.9% of the total. Only one had consultant obstetric cover; the rest were general practitioner units. None had anaesthetic consultant cover and patients requiring operative delivery were either transferred to a consultant unit or treated by a flying squad. That such units have a part to play in the obstetric services in remote areas is not in doubt, but as far as anaesthetic services are concerned, they will not be considered further in this paper.

Caesarean section

This operation was, of course, the most common requiring anaesthesia. In all, there were 8311 sections or 13.3% of all deliveries (Table 2). In Group A hospitals, the Caesarean section rate was 15.2%, in Group B, 12.2%, and in Group C 11.1%. Given the wide differences in the social and geographical backgrounds of the hospital populations, the section rate was not unduly different between hospitals.

General anaesthesia

General anaesthesia was administered to 5348 patients for Caesarean section. It is, unfortunately, not known how many of these were elective and how many were emergency sections. In any event, general anaesthesia was given to 64.3% of patients undergoing Caesarean section.

A further 134 patients had forceps delivery performed under general anaesthesia. The great majority of these procedures are done either with pudendal block or with epidural block, if it has been established during labour for relief of pain.

Table 1. Classification of hospitals

	No. of hospitals	No. of deliveries	Total (%)
Group A (>2500)	11	37 579	60.4
Group B (1500–2499)	9	16 331	26.2
Group C (1000–1499)	4	5290	8.5
Group D (<1000)	17	3057	4.9

Table 2. Caesarean sections

	No. of sections	Rate (%)	General (%)	Epidural (%)
Group A	5729	15.2	58	42
Group B	1997	12.2	81	19
Group C	585	11.1	67.7	32.3
Total	8311	13.3	5348	2963

Table 3. Epidurals during labour

	No. of deliveries	% of all deliveries	Range (%)
Group A	8399	22.4	0–38
Group B	1006	6.2	0–19.7
Group C	573	10.8	0–23.3
Total	9978	16	0–38

Epidural blockade

Epidural blockade was used for Caesarean section in 2963 patients, that is 35.7% of all sections. There was an enormous inter-hospital variation in the use of epidural block for Caesarean section, from 0% to 81.5%. It might be thought that the larger hospitals would do more epidurals than the smaller ones, but this was not always so. In Group A hospitals, 42% of patients were sectioned under epidural blockade, compared to 19% in Group B and 32.3% in Group C. In one hospital with only 1274 deliveries, 106 of 162 Caesarean sections (65.4%) were done with epidural blockade. Only three hospitals (two in Group B and one in Group A) gave no epidurals for this operation.

Epidural blockade for relief of pain in labour (Table 3)

Epidural block for pain relief in labour was used in 9978 mothers, that is 16% of all deliveries. In Group A, the epidural rate in labour was 22.4% (range 0–38%), in Group B it was only 6% (range 0–19.7%) and in Group C, 10.8% (range 0–23.3%). The relatively high rate in Group C is due to the hospital mentioned above, which achieved an epidural rate of 23.3% in their 1274 deliveries.

Ten hospitals (eight in Group A and two in Group B) offered a full epidural service, available 24 hours a day on demand. Nine claimed to have a partial service, though four of these dealt with fewer than 5% of the mothers delivered. There was therefore little or no service available in nine hospitals (one in Group A, six in Group B and two in Group C).

Table 4. Consultant anaesthetic sessions

	Average weekly consultant sessions	Range
Group A	8	0–10
Group B	5	0–10
Group C	1	0–2

Consultant anaesthetist cover (Table 4)

In terms of officially allocated sessions, 19 hospitals had nominated consultants and five had none. In Group A, of the 11 hospitals seven had 10 weekly sessions, one had eight sessions, one had seven, one had four and one had none. This last with 2600 deliveries a year also did not have a junior anaesthetist immediately available (see below) for emergency cover. For obvious reasons their epidural rate was very much lower than the group average.

In Group B, the number of consultant sessions varied from 0–10, with an average of five. In Group C, two hospitals had two sessions and two had none.

Junior anaesthetic cover (Table 5)

In nine hospitals (eight in Group A and one in Group B) there was an anaesthetic junior always immediately available with no other duties. In three hospitals it was said that the junior would take not more than 15 minutes to reach the

Table 5. Junior anaesthetic cover

	Immediate	Up to 15 minutes	Up to 30 minutes	> 30 minutes
Group A	8	1	0	2
Group B	1	1	5	1
Group C	0	1	1	2

operating theatre/labour ward, after receiving an emergency call. In six hospitals the junior's other duties, and/or the remoteness of the maternity unit, could involve a wait of up to 30 minutes. In five hospitals (two in Group A, one on Group B and two in Group C) it could take more than 30 minutes for the junior on emegency call to reach the maternity unit. One hospital in Group B had no junior anaesthetic staff, and it could sometimes take more than 30 minutes for the consultant to arrive.

In most of the hospitals, only juniors with more than 1 year's experience were on call for obstetrics, although about 30% had to use some with only 6 months' experience of anaesthesia.

Help for the anaesthetist

During the preparation for, and the induction of, anaesthesia, the anaesthetist had the assistance of either a midwife or an operating department orderly. Occasionally, the anaesthetists felt that the help was of a very inexperienced nature.

Midwife instruction in epidural blockade

In only four of the 24 hospitals were midwives not instructed in the nursing management of an epidural block given during labour. However, as there was no epidural service available in five others, such instruction could only have been theoretical. The questionnaire also asked whether the anaesthetic department would welcome midwives giving top-up epidural injections if they had received appropriate instructions; 16 were in favour and eight against.

General assessment of the anaesthetic services

Each anaesthetic department was asked its opinion on whether their local arrangements were satisfactory or not, giving their reasons if they were unsatisfactory. Eleven were satisfied and 13 were not. The commonest causes for dissatisfaction were shortage of staff, both medical and nursing, and remoteness of the maternity unit.

In making an objective assessment, taking into account the number of consultant sessions relative to the number of deliveries, the availability of junior staff and the epidural service offered, one of the authors (D.B.S.) considered that only six hospitals (all in Group A) were completely satisfactory. In the six hospitals in which it could take over 30 minutes for the emergency anaesthetist to arrive, a potentially dangerous situation was present.

Discussion

So far as we are aware, this enquiry is the most complete recent survey of obstetric anaesthetic practice in Scotland. The purpose of the enquiry was to assist the NMCC Working Group to examine current standards of practice and identify areas of deficiency which could affect the safety of overall standards of obstetric anaesthetic practice in Scotland.

Scotland is a large country with a relatively small population (5.5 million). This means that there is a comparatively large number of very small hospitals undertaking obstetric care. However, the 17 hospitals delivering less than 1000 mothers a year (the highest in any hospital was only 557), were responsible for less than 5% of the total births in 1982. Supplying an anaesthetic service to hospitals as small as this is clearly not practical. Patients who require emergency surgery are either transferred or anaesthetised locally by the flying squad or by a general practitioner anaesthetist.

Hospitals with less than 2500 deliveries a year also present difficulties in arranging a satisfactory anaesthetic service. The amount of work to do is not great, so the anaesthetist frequently has other duties which may conflict with those in the maternity unit. The problem is often compounded by the fact that many maternity units (even some large ones) are quite remote from the nearest general hospital, where the other anaesthetic duties lie.

In spite of all these difficulties, it is reassuring to note that 60% of all deliveries take place in Group A hospitals, i.e. those with more than 2500 deliveries. Given that most of these hospitals have adequate staff and facilities, their practice may be considered as close to optimal. It is of interest, therefore, that they have the highest epidural rate, both for the relief of pain in labour and for Caesarean section. In smaller hospitals, the epidural rate depends greatly on the personal enthusiasm of consultants, though remarkably high rates are achieved. Epidural blockade is an essential part of modern obstetric practice and it should not be considered as an optional extra.

The main concern of the NMCC Working Group was the standard of obstetric anaesthetic practice in relation to maternal morbidity and mortality. The maternal mortality rate in Scotland is not high, and anaesthesia is responsible for only 2–3 deaths per annum. However, there must be concern regarding the arrangements for emergency anaesthesia in many of our obstetric units. The longer it takes for an anaesthetist to arrive at an emergency, the more fraught is the situation. Where there is no anaesthetist on site at the unit, an emergency anaesthetic has to be given to a patient who has not been previously seen or prepared by the anaesthetist. To maximise safety, an on-site anaesthetist is essential. Though this is not always possible, especially in the smaller units, more consideration could be given to the location of anaesthetic staff, both junior and senior. An anaesthetist's presence in the labour ward can often avoid the need for unsafe emergency anaesthesia.

Anaesthesia, 1986, Volume 41, pages 375–381

Atracurium infusions in patients with renal failure on an ITU

R. B. GRIFFITHS, JENNIFER M. HUNTER AND R. S. JONES

Summary

An infusion of atracurium was used (after an initial bolus dose) in five patients with renal and respiratory failure, who were being subjected to intermittent positive pressure ventilation before renal dialysis. Neuromuscular function was monitored by the train-of-four pattern of stimulation. In three patients, atracurium 0.6–0.7 mg/kg/hour completely abolished the twitch response; in the other two (both of whom were markedly oedematous) this did not occur, even with a dose of 1.0 mg/kg/hour, although satisfactory clinical control was obtained. In all patients, there was rapid spontaneous recovery when the infusion was stopped. One patient convulsed, but plasma laudanosine levels taken at this time were below the toxic range. Atracurium infusions appear to provide easily controllable neuromuscular blockade in the intensive therapy unit, although these preliminary results suggest that larger doses may be required in the oedematous patient.

Key words

Neuromuscular relaxants; atracurium.
Anaesthetic techniques; relaxant infusion.

Patients with respiratory failure are frequently subjected to intermittent positive pressure ventilation (IPPV) in the intensive therapy unit (ITU). Central depressant drugs are often given to sedate the patient, but a long acting muscle relaxant is sometimes required to facilitate artificial pulmonary ventilation. Relaxants such as alcuronium or pancuronium, which are frequently used for this purpose, have the disadvantage of being excreted, at least in part, by the kidney;[1] therefore, if the patient is also in renal failure, cumulation of these drugs may occur. This cumulation may hinder 'weaning' from ventilation when the patient's condition has improved.

The new non-depolarising muscle relaxant atracurium breaks down spontaneously in the plasma by Hofmann elimination and has been shown to be superior to other non-depolarising drugs in patients with chronic renal failure undergoing surgery,[2] because its lack of cumulation ensures a rapid and complete recovery. The short half life of the drug (approximately 21 minutes[3]) necessitates frequent bolus doses and this would seem to be impracticable in the intensive care unit. Infusions of atracurium have been used in the operating theatre[4] and it was decided to investigate this method of administration in patients with renal failure (prior to dialysis), who also required IPPV. Particular attention was paid

---

R.B. Griffiths, MB, ChB, FFARCS, Senior Registrar, Jennifer M. Hunter, MB, ChB, FFARCS, Senior Lecturer,* R.S. Jones, MVSc, DR MED VET, FRCVS, DVA, Senior Lecturer, General Intensive Therapy Unit, Ward 11Z, 11th Floor, Royal Liverpool Hospital, Prescot Street, Liverpool, L69 3BX.

*Correspondence should be addressed to Dr J.M. Hunter, University Department of Anaesthesia, Royal Liverpool Hospital, Prescot Street, P.O. Box 147, Liverpool, L69 3BX.

0003–2409/86/040375 + 07 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

to the rapidity of recovery once the infusion had been stopped. The study had the approval of the Committee of Safety of Medicines and the Hospital Ethical Committee.

Methods

Five patients were studied. All needed immediate artificial ventilation on admission to the ITU and all were in acute renal failure. Neuromuscular function was monitored using the train-of-four (TO4) pattern of stimulation. The precise method has been described in detail elsewhere.[5] On admission to the ITU, each patient had been established on a continuous infusion of morphine (4–10 mg/hour) to produce satisfactory sedation.

Once the TO4 monitoring equipment had been set up and control values obtained, a bolus dose of atracurium 0.6 mg/kg was administered via a central vein. In the one patient who was not already undergoing IPPV and who did not have a tracheal tube *in situ*, ventilation was commenced and tracheal intubation effected (using a small dose of methohexitone as an adjuvant to cover the procedure).

Immediately after the bolus dose of atracurium had been given, an infusion of the drug was started, initially at a rate of 0.6 mg/kg/hour, also into a central line. The infusion of morphine continued throughout the period of monitoring and doses of midazolam (1–3 mg) were also given as necessary, to maintain good sedation.

The TO4 twitch response was monitored continuously until a stable state had been reached. If the height of the first twitch of the TO4 A', had not fallen below 20 percent of control 30 minutes after starting the infusion, the rate of the infusion was increased by 0.1 mg/kg/hour every 30 minutes until this had been achieved. When A'/A had been less than 20 percent for at least one hour, the monitoring equipment was switched off, although the hand was left in the splinted position. The height of the TO4 was then checked at regular intervals throughout the infusion and the dose adjusted accordingly.

Atracurium was administered in this way for between 14 and 37 hours; during this time, systemic arterial and pulmonary artery monitoring lines were set up and a dialysis cannula inserted. Once the condition of the patient had been stabilised, the infusion was found to be no longer necessary; sedation alone was sufficient, and before dialysis commenced the infusion was discontinued. Continuous monitoring of the TO4 was recommenced immediately before the infusion was stopped and was only terminated when recovery of the TO4 was judged to be satisfactory. The monitoring equipment was then removed and dialysis commenced.

Table 1. Acid base data from the patients studied, obtained immediately before the infusion of atracurium was commenced

	$F\text{io}_2$	pH	$P\text{aco}_2$ kPa	$P\text{ao}_2$ kPa	Base excess m mol/litre	Shunt
Case 1	0.6	7.24	5.5	11.2	−9.2	25%
Case 2	0.5	7.42	4.0	7.5	−0.9	30%
Case 3	0.7	7.15	7.5	10.9	−8.2	25%
Case 4	0.4	7.45	11.5	8.8	−0.7	20%
Case 5	0.4	7.40	3.5	10.3	−7.5	16%

Table 2. Biochemical data from the patients studied, obtained immediately before the infusion of atracurium was commenced. (Normal values in brackets)

	Na^+ mmol/l (130–150)	K^+ mmol/l (3.6–5.4)	HCO_3 mmol/l (20–30)	Urea mmol/l (3.0–7.0)	Creatinine μmol/l (60–110)	Total bilirubin μmol/l (2.0–17)	SGOT U/l (7–45)	γ GT U/l (0–65)	Alkaline phosphatase U/l (35–130)
Case 1	141	5.8	16	52.8	763	45	3	17	56
Case 2	141	3.4	28	29.1	1014	6	57	13	60
Case 3	139	4.4	25	40.0	944	10	13	140	193
Case 4	133	4.7	28	26.5	451	132	68	48	194
Case 5	132	3.3	22	11.5	673	122	2000	21	173

Case histories

An outline history of each of the five patients is given below. Results of blood gas analysis, liver function and electrolyte values for each patient immediately prior to the start of the atracurium infusion are given in Tables 1 and 2. All the patients required inotropic support (with dopamine) during the periods of the infusion.

Case 1. A 60-year-old man was admitted to another hospital following a fall. His injuries, which included avulsion of the duodenum, pancreas and common bile duct, and a torn right hepatic artery, necessitated transfusion of 19 units of blood before and during emergency laparotomy. A choledochojejunostomy was formed and the right hepatic artery ligated. An ECG immediately prior to laparotomy revealed a hyperacute anteroseptal myocardial infarction. Postoperatively, IPPV was continued because of poor respiratory function complicating cardiovascular instability. Renal function deteriorated progressively, but after 2 weeks the patient's cardiovascular condition was stable enough to permit transfer for haemodialysis, although he still required IPPV. He had by then developed considerable peripheral oedema.

He was admitted to the atracurium trial. The infusion was continued for 14.5 hours and dialysis was started the following day. Recovery thereafter was stormy but the patient was able to leave the ITU 20 days after admission. He was eventually discharged from hospital with good respiratory and renal function.

Case 2. A 55-year-old man, who was on haemodialysis for chronic renal failure, was admitted for cadaveric renal transplantation. The surgical procedure was uneventful, but on the first postoperative day a myocardial infarction with pulmonary oedema resulted in a cardiac arrest. Resuscitation was prompt and good cerebral function returned. Transfer to the ITU was necessary to continue IPPV, in order to maintain adequate oxygenation and to avoid hypotension. Morphine combined with muscular relaxation was considered necessary.

An infusion of atracurium was set up in accordance with the trial protocol. Urine output from the transplanted kidney was 700 ml in 24 hours following an injection of frusemide 500 mg, but a rising serum creatinine indicated the need for dialysis. The atracurium infusion was discontinued before dialysis was commenced, after a total of 22 hours 16 minutes.

With ultrafiltration, a substantial negative fluid balance occurred; this resulted in an improvement in the pulmonary oedema. However, continued muscular relaxation was found necessary for adequate oxygenation and a second infusion of atracurium was started 2 hours after haemodialysis (and some 7 hours after the first infusion had been discontinued) at a rate of 0.6 mg/kg/hour. This was continued for a further 78 hours, but neuromuscular monitoring was not carried out on this occasion though it was noted that, after stopping the second atracurium infusion, recovery of muscle power was rapid. The data from this infusion are not recorded in the results in Table 3.

Six days after admission to the ITU respiratory function was adequate and the nasotracheal tube was removed. The following day the patient was returned to the renal unit and 4 weeks later was discharged home with good renal function.

Case 3. A 42-year-old man with mycoplasma pneumonia was admitted to another hospital. Lobar consolidation and rapidly increasing pulmonary oedema produced severe hypoxia. On transfer to the ITU of that hospital he suffered a cardiorespiratory arrest. Resuscitation was successful and recovery of cardiovascular and cerebral function was good. However, IPPV was necessary to maintain adequate oxygenation. Renal function deteriorated progressively after this event and 17 days following his admission the patient was transferred for haemodialysis. Poor synchronisation of IPPV indicated the need for muscular relaxation in addition to sedation and an infusion of atracurium according to the trial protocol was set up. Haemodialysis was started after discontinuing the atracurium which was used for a total of 17 hours 25 minutes. The subsequent history was stormy, but the patient was discharged from the ITU to the care of the nephrology ward 5 weeks after admission for haemodialysis.

Case 4. A 35-year-old woman was admitted to another hospital with atypical pneumonia. Respiratory failure within 24 hours required IPPV of the lungs. After a further week, deteriorating renal function necessitated peritoneal dialysis but, although this was initially effective, peritonitis made it necessary to transfer the patient to this ITU for haemodialysis after 2 weeks. On arrival, there was marked pulmonary oedema and cardiovascular instability. Sedation with mor-

Table 3. Details of the rate and duration of the infusion of atracurium in each of the five patients are given, together with the total dose of atracurium administered during the period of the study. The height of A′/A and D′/A′ on stopping the infusion, the subsequent time (minutes) over which monitoring continued and the final values recorded for A′/A and D′/A′ are also included

Patient	Mean infusion rate (mg/kg/hour)	Duration of infusion		Total dose (bolus + infusion, mg)	A′/A + D′/A′ on stopping infusion	Time from completion of infusion to stopping monitoring (minutes)	A′/A + D′/A′ on stopping monitoring
		Hours	Minutes				
1	1.0	14	30	1270	A′/A = 56% D′/A′ = 11%	105	A′/A = 100% D′/A′ = 100%
2	0.6	22	16	1088	No TO4	60	A′/A = 100% D′/A′ = 67%
3	0.6	17	25	890	No TO4	75	A′/A = 120% D′/A′ = 78%
4	1.0	23	30	1729	A′/A = 85% D′/A = 82%	50	A′/A = 92% D′/A′ = 91%
5	0.7	36	50	1295	No TO4	47	A′/A = 39% D′/A = 100%

phine allowed IPPV to continue, but caused a fall in systemic arterial pressure. A muscle relaxant was therefore thought to be indicated, and the patient was admitted to the atracurium trial. During the first 24 hours of infusion, large volumes of fluid had to be infused to maintain the pulmonary capillary wedge pressure (PCWP) and marked peripheral oedema developed. This was associated with marked resistance to atracurium, even administered at a dose of 1.0 mg/kg/hour. The infusion was stopped before the first haemodialysis. Further muscle relaxation was required later that day, however, to facilitate adequate respiratory exchange and bolus doses of atracurium 20–25 mg were used to a total of 1085 mg over the next 93 hours; at this stage the total dose administered was 2814 mg. The patient developed generalised twitching, while still receiving bolus doses of atracurium, which proved almost impossible to control. Injections of phenobarbitone and phenytoin, together with an infusion of magnesium sulphate and diazepam 20 mg/hour, were only partly successful in controlling the fits. Two days after the fits started the atracurium was stopped. Arterial blood was taken to assess laudanosine levels 2, 6, and 24 hours after the last dose of atracurium. It was 36 hours after stopping the bolus injections of atracurium before it was possible to withdraw the anticonvulsive therapy. Pneumonia and toxaemia, however, progressed and 26 days after admission to hospital the patient died.

Case 5. A 21-year-old woman was admitted to another hospital several days after taking an overdose of paracetamol. On admission she was breathing spontaneously but was unconscious and hypothermic (rectal temperature 32°C). The blood paracetamol level was 55 mg/litre. Hepatic failure was obvious, with a prolonged prothrombin time and raised serum bilirubin. A serum amylase of 1335 IU/litre indicated pancreatitis. Deteriorating renal function over the next 3 days prompted transfer to the ITU. On arrival, a tracheal tube was passed and IPPV was instituted because of deteriorating respiratory function. The patient was hypovolaemic, with a low PCWP, but despite adequate intravenous infusion, low-dose dopamine and mannitol there was virtual anuria. Poor synchronisation on IPPV, despite an infusion of morphine, was thought to indicate a need for muscular relaxation, and the patient was admitted to the atracurium trial. *Staphylococcus aureus* and a Gram negative bacillus were cultured from sputum within 24 hours and treatment with tobramycin and flucloxacillin was commenced and continued during the time of the atracurium infusion. Repeated transfusions of blood products were required and acceptable cardiovascular stability was obtained only at the expense of marked peripheral oedema. The infusion of atracurium was stopped after 36 hours and peritoneal dialysis was instituted. Later that day, the infusion of morphine was also discontinued as the patient had made no meaningful response to stimuli for 24 hours. Brain stem death was diagnosed 4 days later and intensive therapy was withdrawn. Post-mortem examination revealed global cerebral necrosis as well as liver and renal necrosis.

Results

The mean rates of infusion, duration of infusion and total dose of atracurium given to each of the five patients during the course of the study is given in Table 3.

In three of the five patients, the initial bolus dose of atracurium (0.6 mg/kg) produced complete ablation of the TO4. In patients 1 and 4, however, both of whom showed marked peripheral oedema, the TO4 persisted after this dose, and satisfactory control (in terms of twitch response) was not subsequently achieved by an infusion of atracurium 0.6 mg/kg hour. Therefore, the dose was increased in steps of 0.1 mg/kg/hour every 30 minutes, up to the maximum defined by the clinical trials certificate (1.0 mg/kg/hour). In patient 1, even this dose only reduced the ratio of the first twitch to control (A′/A) to a minimum of 56 percent and the ratio of the last to the first (D′/A′) to 11 percent, the corresponding figures being 38 and 40 percent in patient 4.

In the other patients (2, 3, and 5) ablation of the TO4 was produced by the initial bolus dose. Patients 2 and 3 then received atracurium 0.6 mg/kg/hour by infusion for over 17 and 22 hours respectively and no response to the TO4 was seen during that time. Patient 5 required atracurium 0.7 mg/kg/hour to ablate the TO4 and this was achieved for almost 37 hours. The mean infusion times in the five patients was 22 hours 54 minutes. The mean total dose of atracurium given (bolus plus infusion) was 1254 mg (range 890–1729 mg).

Recovery of the TO4 appeared to be rapid after the infusion was stopped, and as straightforward in cases 1, 2 and 4. The other two cases, however, showed different patterns (possibly associated with difficulties in monitoring for long periods—see Discussion). In case 3, recovery of the ratio A′/A was to more than 100 percent; in case 5, A′/A showed poor recovery but D′/A′ reached 100 percent (Table 3). The mean heights of A′/A and D′/A′ (SEM) for the five patients at 5 minute intervals after stopping the infusion until the end of the study are given in Fig. 1.

It was not routinely possible to measure serum laudanosine levels in this study. In patient 4, however, who developed status epilepticus after large doses of the drug, it was thought necessary to do so. The results showed that 2 hours after the last bolus of atracurium had been given, the plasma laudanosine level was 0.74 μg/ml; at 6 hours it was 0.6 μg/ml and at 24 hours it was 0.43 μg/ml.

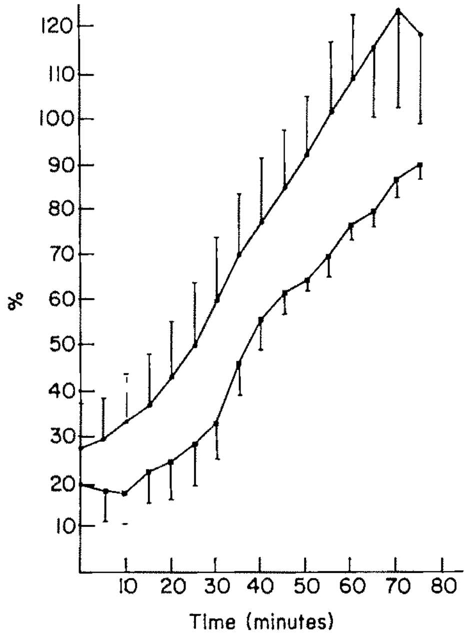


Fig. 1. Mean height of A′/A (●) and D′/A′ (■) with SEM, at 5-minute intervals after stopping the atracurium infusion.

None of these patients showed any marked cardiovascular changes after the bolus dose of atracurium 0.6 mg/kg. The patients all had some degree of cardiovascular instability and were receiving intravenous infusions of inotropic agents. Nevertheless, 3 minutes after the bolus dose there was little change in blood pressure or pulse rate. Similarly, there were no cardiovascular changes during the study that could be attributed to the infusion. No evidence of histamine release was seen after the bolus dose of atracurium, or at any point during the infusion of the drug.

Discussion

Non-depolarising muscle relaxants are frequently used in an ITU, especially in patients with poor lung compliance, to facilitate IPPV. In the United Kingdom, the two most widely used agents in these circumstances are probably pancuronium and alcuronium. Both, however, may cause residual paralysis in patients with renal failure. Infusions of muscle relaxants have not been routinely used in the ITU because of the potential problem of cumulation. However, with the introduction of the two shorter acting relaxants, atracurium and vecuronium (which have a shorter half life, even in renal failure) an infusion may well be suitable, especially as the need for repeated doses makes their use in bolus form impracticable.

Muscle relaxants are not often required once the patient has been stabilised and monitoring lines have been inserted; sedatives such as morphine and a benzodiazepine are then usually sufficient. Moreover, dialysis causes alterations in circulating volume and loss of drug can occur through the membrane. For these reasons, the infusion was started soon after the admission of the patient to the ITU and the study was completed before dialysis commenced.

All five patients were extremely ill on admission (ASA 4–5) and all were in renal failure, but the degree of fluid overload varied with each patient. This variability probably affected the amount of atracurium required to produce satisfactory neuromuscular blockade. Thus, patients 1 and 4, who were grossly oedematous, received atracurium 1.0 mg/kg/hour without complete neuromuscular block, though both these patients were well controlled clinically.

Oedema can make mechanical methods of neuromuscular monitoring more difficult;[6] in practice, it may be a problem to stimulate the ulnar nerve at the wrist adequately due to local swelling. In patient 5, the increasing oedema which developed during the course of the study may explain the fact that the ratio A′/A did not return to 100 percent once the infusion was stopped, although the ratio D′/A′ reached almost 100 percent and the patient seemed to have good muscle tone. Conversely, in patient 3 an improvement in the peripheral circulation may have been responsible for the increased height of A′/A′; the hand was warmer and well perfused by the end of the monitoring period. Indeed, because of the practical problems of mechanical monitoring of neuromuscular function over many hours, when it is impossible to maintain the same position of the hand, D′/A′ may well be a better indication of recovery than A′/A.

It was unfortunate that serum laudanosine levels could not be measured in all patients during this study. Laudanosine is the main metabolite of atracurium in humans,[7] and is excreted by the kidney. Concern has been expressed that cumulation of this substance could occur in patients with renal impairment,[8] especially as this substance has been shown to produce epileptiform seizures in dogs in large doses.[9] For this reason, plasma laudanosine levels were measured in patient 4 when status epilepticus developed whilst still receiving bolus doses of the drug every 2 hours. The levels were, however, well below the toxic level necessary to cause convulsions[10] (17 μg/ml) and there were other causes for cerebral irritability in this patient, including hypoxia ($Pa\text{O}_2 = 8$ kPa) and viral encephalitis.

No evidence of histamine release was seen in any of the five patients during the period of the infusion of atracurium, nor was any acute change in cardiovascular status seen during the study which could have been attributable to the infusion of the drug.

We conclude that an infusion of atracurium may be useful for facilitating IPPV in patients with renal failure on an ITU. However, the administration rate needs adjusting according to the individual response. Monitoring by train-of-four stimulation is suitable for this purpose. Patients who are grossly oedematous may require larger doses of the drug.

Acknowledgments

We are grateful to all the nursing staff on the Intensive Therapy Unit, Royal Liverpool Hospital for their great patience during this study and also to Phillip Locke for technical assistance. The study was funded in part by the Wellcome Foundation who also estimated the plasma laudanosine levels in patient 4.

References

1. Buzello W, Agoston S. Kinetics of intercompartmental disposition and excretion of tubocurarine, gallamine, alcuronium and pancuronium in patients with normal and impaired renal function. *Anaesthesist* 1978; **27**: 319–21.
2. Hunter JM, Jones RS, Utting JE. Use of atracurium in patients with no renal function. *British Journal of Anaesthesia* 1982; **54**: 1251–8.
3. Ward S, Neill EAM. Pharmacokinetics of atracurium in acute hepatic failure (with acute renal failure). *British Journal of Anaesthesia* 1983; **55**: 1169–72.
4. Eagar BM, Flynn PJ, Hughes R. Infusion of atracurium for long surgical procedures. *British Journal of Anaesthesia* 1984; **56**: 447–52.
5. Hunter JM, Jones RS, Utting JE. Use of atra-

curium during general surgery monitored by the train-of-four stimuli. *British Journal of Anaesthesia* 1982; **54:** 1243–50.

6. Hunter JM, Kelly JM, Jones RS. Difficulties with neuromuscular monitoring. *Anaesthesia* 1985; **40:** 916.
7. Stenlake JB, Waigh RD, Urwin J, Dewar GH, Coker GG. Atracurium: conception and inception. *British Journal of Anaesthesia* 1983; **55:** 3S–10S.
8. Miller RD. Effect of renal disease. *Clinics in Anaesthesiology* London: W.B. Saunders, 1985; **3:** 307–13.
9. Mercier J, Mercier E. Action de quelques alcaloides secondaires de l'opium sur l'électrocorticogramme du chien. *Comptes Rendus des Séances de la Société de Biologie* 1955; **149:** 760–2.
10. Chapple DJ, Miller AA, Wheatley PL. Neurological and cardiovascular effects of laudanosine in conscious and anaesthetised dogs. *Anesthesiology* 1985; **63:** A311.

Anaesthesia, 1986, Volume 41, pages 382–385

Profound atracurium induced neuromuscular blockade

A comparison of evoked reversal with edrophonium or neostigmine

W.R. CASSON AND R.M. JONES

Summary

Speed of reversal of profound atracurium induced neuromuscular blockade following edrophonium (0.5 or 1.0 mg/kg) or neostigmine (0.04 or 0.08 mg/kg) was measured using the train-of-four pattern of nerve stimulation. In all patients adequate clinical reversal was present when the ratio of the strength of the fourth to the first twitch (T4 ratio) was 0.5. Both doses of edrophonium were associated with a significantly faster speed of reversal than the smaller dose of neostigmine ($p<0.05$ in both cases). However, the larger dose of neostigmine was associated with a reversal time approaching that of edrophonium. Possible explanations for these findings are discussed in terms of contemporary theories of neuromuscular pharmacology.

Key words

Neuromuscular relaxants; atracurium.
Antagonists, neuromuscular relaxants; edrophonium, neostigmine.

Edrophonium is a synthetic, reversible cholinesterase inhibitor. It is now established that in the dose range 0.5–1.0 mg/kg, it is able to produce reliable and sustained antagonism of neuromuscular blocking agents.[1] After spontaneous offset of atracurium induced block to at least 10 percent of control twitch strength, edrophonium promotes more rapid recovery of neuromuscular function than neostigmine.[2] However, if the block is profound this may not be the case.[3] We have compared edrophonium and neostigmine reversal of profound atracurium induced block using clinical observation as well as assessing the degree of residual paralysis using the train-of-four pattern of stimulation.

Methods

After local Ethics Committee approval we studied 20 ASA class 1 unpremedicated adults, scheduled to undergo surgery requiring muscle relaxation. Patients greater or less than 20 percent of their ideal body weight were not studied. Prior to induction of anaesthesia, the left arm was immobilised in a splint and the left thumb was connected to a miniature force transducer, in order to measure isometric contractions of the adductor pollicis.[4] The force of contraction was recorded using a Devices pre-amplifier and a two-channel chart recorder.

An indwelling needle was inserted in a vein on

W.R. Casson, FFARCS, Lecturer, R.M. Jones, FFARCS, Senior Lecturer, Department of Anaesthetics, The United Medical and Dental Schools of Guy's and St Thomas's Hospitals, London Bridge, London SE1.
Correspondence should be addressed to Dr R.M. Jones please.

0003–2409/86/040382 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Table 1. Age, sex and weight characteristics

Dose	*n*	Male	Female	Age (years)	Weight (kg)
Edrophonium, 0.5 mg/kg	5	2	3	26.0 (6.0)	73.0 (19.9)
Edrophonium, 1.0 mg/kg	5	0	5	20.6 (3.1)	63.6 (5.7)
Neostigmine, 0.04 mg/kg	5	2	3	24.0 (2.6)	60.0 (9.0)
Neostigmine, 0.08 mg/kg	5	1	4	22.6 (2.6)	58.6 (8.2)

Table 2. Times from anticholinesterase administration to achievement of a T4 ratio of 0.5

Dose	Time (seconds)	Range (seconds)
Edrophonium, 0.5 mg/kg	189 (195)	35–530
Edrophonium, 1.0 mg/kg	225 (126)	92–405
Neostigmine, 0.04 mg/kg	523 (243)	249–795
Neostigmine, 0.08 mg/kg	346 (160)	245–630

the dorsum of the right hand and anaesthesia was induced using thiopentone in a dose 20 percent greater than that required to abolish the eyelash reflex. The needle was then flushed with normal saline. The left ulnar nerve was stimulated by supramaximal 0.2 ms square wave impulses, delivered in a train-of-four pattern at 2 Hz for 2 seconds via surface electrodes at the wrist, repeated at 12 second intervals (Myotest). Immediately following a control train, atracurium, 0.5 mg/kg was injected and flushed in with normal saline. The patient's lungs were ventilated with 50 percent nitrous oxide in oxygen, supplemented with 1 percent halothane and the trachea was intubated 3 minutes after injection of the relaxant or when there was no recordable first twitch. Ventilation was via a Bain type coaxial breathing system with a fresh gas flow designed to maintain normocarbia. The concentration of halothane was reduced after intubation to 0.5 percent and that of nitrous oxide increased to 66 percent.

The patients were randomly divided into four groups to receive edrophonium (0.5 or 1.0 mg/kg) or neostigmine (0.04 or 0.08 mg/kg) to reverse the block. When surgery was completed, and after the return of the first recordable response of adductor pollicis to ulnar nerve stimulation ($T1 < 2$ percent of control), the chosen anticholinesterase was injected intravenously with a suitable dose of atropine (0.6–1.2 mg). The time from then to the point where the ratio of the fourth to the first twitch (T4 ratio) reached 0.5 was recorded. At this point, spontaneous ventilation was adequate and all patients appeared clinically to be adequately reversed. They were then turned on their side, and their tracheas extubated before being taken to the recovery ward. All patients were carefully observed for any signs of residual neuromuscular blockade for at least 2 hours.

Statistical analysis was with the unpaired *t*-test.

Results

Results are expressed as mean (SD) where applicable. The age, sex and weight characteristics of the patients are shown in Table 1. Recovery times in the four groups are shown in Table 2.

There was a wide variation in recovery times in all four groups, but there was no significant difference between the recovery times following the two doses of edrophonium, nor between the two doses of neostigmine. However, the times following the smaller dose of neostigmine (0.04 mg/kg) were significantly longer than those following both the smaller ($p < 0.05$) and the larger ($p < 0.05$) doses of edrophonium. Although recovery times after the larger dose (0.08 mg/kg) of neostigmine tended to be longer than those following edrophonium, this was not statistically significant. No patient exhibited any signs of residual neuromuscular blockade by any of the standard criteria, such as sustained head lift or strength of hand grip; all were able to maintain their own airway and cough forcefully immediately after extubation.

Discussion

The use of edrophonium in comparatively large doses (0.5–1.0 mg/kg) to reverse residual neuromuscular blockade has gained increasing popularity. Administered in this dose range, it has a pharmacokinetic profile similar to that of neostigmine[5] (ensuring sustained reversal of block) and it appears to possess a number of distinct advantages. Atropine requirements are less using edrophonium,[1] which presumably reflects its more specific action at the neuromuscular junction and its comparative lack of muscarinic effects. It also appears that if spontaneous recovery of twitch strength, either using single twitch or the first twitch of a train-of-four as the criterion, to at least 10 percent of control has occurred, edrophonium causes a considerably more rapid and complete recovery of neuromuscular function.[1,2] These factors have led one commentator to suggest that edrophonium may now be the anticholinesterase of choice when reversing non-depolarising neuromuscular blockade.[6]

However, a recent report utilising single twitch monitoring has suggested that, if the degree of block is profound, with single twitch depression greater than 90 percent, neostigmine acts more rapidly than edrophonium in reversing vecuronium or pancuronium induced blockade. The same study also reported that when reversing a dense atracurium induced block, there was no difference between the two anticholinesterases.[3] These observations support the previously noted possibility that the speed and completeness of reversal using different anticholinesterases varies according to the particular relaxant which has been administered.[7] Differences such as this may be more easily demonstrated using a different mode of nerve stimulation than the single twitch.

The train-of-four pattern of stimulation[8] has gained wide acceptance as a method of quantifying neuromuscular blockade. One practical advantage of this mode of stimulation is that each train acts as its own control and it is therefore unnecessary to know the initial twitch strength before administering the neuromuscular blocker. It has previously been demonstrated that if the ratio of the fourth to the first twitch (T4 ratio) is 0.5 or more after atracurium induced blockade, then this is associated with a clinically safe degree of reversal.[2] Our study has again confirmed this observation as none of our patients demonstrated any symptoms which could be attributed to residual curarisation.

Whatever method of monitoring neuromuscular blockade is used, it is essential that it should allow for the clear definition of safe reversal of block. It has been demonstrated that a single twitch may not be reduced, even though 75 percent of the cholinergic receptors are occupied.[9] We therefore compared speed of reversal using train-of-four, rather than single twitch stimulation. Using this method we have demonstrated that, overall, edrophonium causes a more rapid reversal of a dense atracurium induced block to clinically safe levels. Although it appears that doubling the dose of edrophonium from 0.5 to 1.0 mg/kg does not reduce the time to safe reversal, if the dose of neostigmine is doubled from 0.04 to 0.08 mg/kg, then the speed of reversal approaches that obtained using edrophonium.

There is also evidence that reversal with edrophonium is quantitatively different from that with neostigmine. It appears that the former has more 'anti-fade' properties than the latter.[2] The evidence for and against a pre- and postjunctional mechanism for fade has been discussed by Bowman.[10] Available evidence appears to favour an action of nondepolarising relaxants on prejunctional receptors or ion channels, so that fade occurs by a reduction in the movement of axoplasmic acetycholine into the vesicles, where it would be available for immediate release. It has also been demonstrated that not only do different degrees of fade occur during spontaneous offset of blockade compared to onset, but that different relaxants cause different degrees of fade at similar ratios of first twitch depression.[11] One explanation for this phenomenon is that each agent has different affinities for prejunctional sites. Similarly, the fact that edrophonium and neostigmine may have a different spectrum of activity at these sites may, at least partially, explain the former's rapid action, particularly when a lessening of train-of-four fade is used as the criterion for reversal.

In conclusion, we have demonstrated that, using the train-of-four pattern of stimulation and clinically safe reversal of neuromuscular blockade as the criteria for adequate antagonism of atracurium, edrophonium 0.5 mg/kg is significantly superior to neostigmine 0.04 mg/kg. Doubling the dose of edrophonium to 1.0 mg/kg does not significantly influence speed of reversal, although doubling the dose of neostigmine to 0.08 mg/kg does improve reversal time, so that it approaches that of edrophonium. Our results suggest that the reversal of muscle relaxants is influenced in clinically important ways by the particular relaxant originally administered, the degree of spontaneous offset present at the time of antagonist administration and the type and dose of antagonist administered. It is also important, when comparing the results of published studies, to be aware that the precise method of monitoring the degree of block present may influence the findings and conclusions of the authors.

References

1. Cronnelly R, Morris RB, Miller RD. Edrophonium: duration of action and atropine requirement in humans during halothane anesthesia. *Anesthesiology* 1982; **57**: 261–6.
2. Jones RM, Pearce AC, Williams JP. Recovery characteristics following antagonism of atracurium with neostigmine or edrophonium. *British Journal of Anaesthesia* 1984; **56**: 453–7.
3. Rupp SM, McChristian JW, Miller RD. Neostigmine antagonizes a profound neuromuscular blockade more rapidly than edrophonium. *Anesthesiology* 1984; **61**: A297.
4. Stanec A, Stanec G. The adductor pollicis monitor-apparatus and method for the quantitative measurement of the isometric contraction of the adductor pollicis muscle. *Anesthesia and Analgesia* 1983; **63**: 602–5.
5. Morris RB, Cronnelly R, Miller RD, Stanski DR, Fahey MR. Pharmacokinetics of edrophonium and neostigmine when antagonizing d-tubocurarine neuromuscular blockade in man. *Anesthesiology* 1981; **54**: 399–402.
6. Crul JF. In: Jones RM, Bergmann H, Lassner J, Otteni JC, Thomson D, eds. *Current European Anaesthesiology, Volume 1*. Chichester: John Wiley, 1985: 38.
7. Jones RM. In: Jones RM, Bergmann H, Lassner J, Otteni JC, Thomson D, eds. *Current European Anaesthesiology, Volume 1.* Chichester: John Wiley, 1985: 34–35.
8. Ali HH, Utting JE, Gray C. Stimulus frequency in the detection of neuromuscular block in humans. *British Journal of Anaesthesia* 1970; **42**: 967–78.
9. Waud BE, Waud DR. The relation between tetanic fade and receptor occlusion in the presence of competitive neuromuscular block. *Anesthesiology* 1971; **35**: 456–64.
10. Bowman WC. The neuromuscular junction: recent developments. *European Journal of Anaesthesiology* 1985; **2**: 59–93.
11. Pearce AC, Casson WR, Jones RM. Factors affecting train-of-four fade. *British Journal of Anaesthesia* 1985; **57**: 602–6.

Anaesthesia, 1986, Volume 41, pages 386–389

Changes in skin thermal clearance during anaesthesia

J. L. SAUMET, C. S. DEGOUTE, A. DITTMAR AND V. BANSSILLON

Summary

Thermal and vascular side effects occuring during general anaesthesia are related to skin blood flow. A new, noninvasive probe which measures skin thermal clearance, a variable closely related to skin blood flow, was used in nine patients under phenoperidine, droperidol, propanidid anaesthesia. Statistically significant increases in skin thermal clearance clearly preceded the drop in mean arterial blood pressure and the rise in skin temperature. It is concluded that general anaesthesia induced an early increase in skin blood flow and that thermal clearance is a better technique than skin thermometry to monitor skin blood flow.

Key words

Skin; blood flow.
Temperature; monitoring.

Cutaneous vasodilatation is one of the thermal and cardiovascular side effects which occur during general anaesthesia. The increase in skin temperature leads to a thermal deficit which is not compensated by shivering. The decrease in peripheral vascular resistance is probably a cause of the fall in mean arterial blood pressure (MABP). The present study was performed in order to analyse the time course and amplitude of skin blood flow (SBF) variations during general anaesthesia in humans. A new, noninvasive probe was used for the measurement of skin thermal clearance, a physiological variable directly related to skin blood flow. Skin temperature, arterial blood pressure and heart rate (HR) were also monitored.

Methods

Subjects and anaesthesia

Nine female patients (35–55 years, 56–71 kg) anaesthetised for lower limb stripping of varicose veins were included in this experiment with their consent. One hour after atropine (1 mg intramuscularly), anaesthesia was induced with 1 mg intravenous phenoperidine and droperidol 5 mg, followed by an intravenous infusion of propranidid till sleep was achieved. The patients were all breathing spontaneously.

Skin thermal clearance and skin temperature

Thermal clearance was recorded using a new non-

J.L. Saumet, Laboratoire de Thermorégulation et de Métabolisme Energétique, CNRS U.A. 181 Université Claude Bernard, 69373 Lyon, Cedex 08, France. C.S. Degoute, Département d'anesthésie-réanimation, Centre Hospitalier Lyon-Sud, 69310 Pierre-Benite, France. A. Dittmar, Laboratoire de Thermorégulation et de Métabolisme Energétique, CNRS U.A. 181 Université Claude Bernard, 69373 Lyon, Cedex 08, France. V. Banssillon, Département d'anesthésie-réanimation, Centre Hospitalier Lyon-Sud, 69310 Pierre-Benite, France.

0003–2409/86/040386 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

invasive probe produced in our laboratory. It is an experimental device and is not commercially available. The probe is a disk, 20 mm in diameter and 4 mm thick, which can be applied to a cutaneous area. The heating device is located at the centre of the probe. The skin temperature gradient between the centre and the periphery of the probe is measured by twelve thermocouples in series. Six hot junctions are located at the centre and six cold junctions on the periphery. The mean skin temperature of the periphery is calculated and recorded. The proportional, derivative and integrative action of an automatic device maintains a constant temperature gradient of 2°C between the centre and the periphery of the probe. The regulation of the gradient, which has an accuracy of 3/100°C, avoids drift phenomena and allows quantitative measurement. The electric power necessary to maintain the constant temperature gradient is dependent on skin blood flow since the heat produced in the centre of the probe is washed out proportionally to blood flow. The probe was calibrated using physical models with thermal conductivity in the same range as human skin.[5] The probe was focused at 1.5 mm in the skin. The results were expressed in thermal conductivity units: $K = 10^{-4}$ cal/cm/°C/second.

Protocol

Patients remained lying on the operating table for 20 minutes before the beginning of anaesthesia. The ambient temperature was 24.5 (SD 0.5°C). Skin thermal clearance and skin temperature were continuously recorded on the first intermetacarpal dorsal space of the left hand. An automatic monitor (Mira Electronique) recorded mean arterial blood pressure and heart rate using the oscillotonometric method. The recording began five minutes before and stopped 20 minutes after the beginning of the first intravenous injection ($t = 0$). Surgical intervention began after the recordings were complete, i.e. $t = 20$ minutes.

Data analysis

Mean skin thermal clearance, mean blood pressure and heart rate and skin temperature were calculated every minute and compared with the mean values before anaesthesia (analysis of variance). A level of $p < 0.05$ was considered significant.

Results

During the pre-anaesthetic period, a fairly steady state of skin thermal clearance 11.10, (SEM 0.24) K, mean blood pressure 113, (SEM 2) beats/min 34.3 (SEM 0.2) °C heart rate 86.6, (SEM 1.6) beats/minute and skin temperature (33.09, SEM 0.13°C) were observed. After the beginning of anaesthesia, statistically significant changes ($p < 0.05$) in these measurements occurred at $t = 1$, $t = 3$, $t = 4$ and $t = 8$ minutes respectively. As shown in Fig. 1, the maximal increase in skin thermal clearance, heart rate and skin temperature were 11.10, (SEM 0.24) K, 113, SEM (2) beats/minute, 34.3, (SEM 0.2) °C and occurred at $t = 4$, $t = 7$ and $t = 20$ minutes respectively. Mean arterial pressure reached its minimum value 70, (SEM, 2.7) mmHg at $t = 5$ minutes.

Figure 2 shows the correlation between mean values of mean arterial blood pressure and heart rate during the 20 minutes of anaesthesia. During this time, no statistically significant correlation was found for mean values of skin thermal clearance versus blood pressure, heart rate or skin temperature.

Maximum skin thermal clearances recorded in our nine patients were significantly correlated with their maximum heart rates ($p < 0.01$) and with their maximum skin temperatures ($p < 0.05$, Fig. 3). No correlation was found between maximum skin thermal clearance and the minimum MABP for our nine patients.

Discussion

The noninvasive and nonradioactive methods used to measure skin blood flow are indirect plethysmography and skin thermometry. Strain or mercury gauge plethysmography can be used only on a limb and is influenced by variations in both skin and muscular blood flows. This method has already been used to analyse vascular changes during heat stress,[2,3] a condition in which muscular blood flow does not change. However, it cannot be extended to general anaesthesia, since anaestheic drugs are pharmacologically active both on skin and skeletal muscle blood flows. Plethysmography using photocell detectors and skin thermometry can be used on any skin surface, but are considered as qualitative techniques at best.

Since the first description of the thermal clearance method and its first application, this method

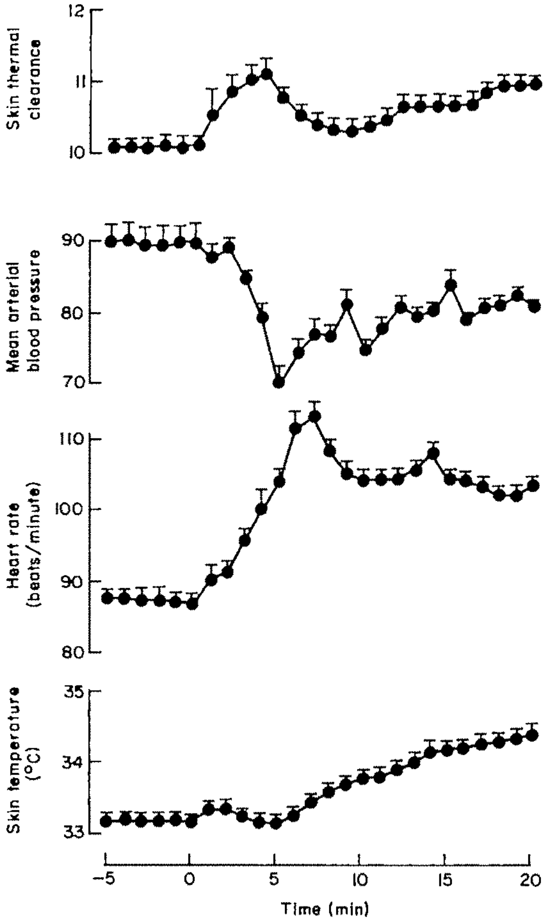


Fig. 1. After phenoperidine droperidol propanidid infusion ($t = 0$) skin thermal clearance, heart rate and skin temperature increase while mean arterial blood pressure decrease. These parameters are represented as mean SEM.

has often been used.[1,4-8] Challoner greatly improved this heat clearance technique.[4] The probe used in the present study differs from that of Challoner in that there is better control of the centre periphery thermal gradient, the possibility of calibration in thermal conductivity units, and the possibility of continuous recording from any part of the body. The heat clearance technique has already been used to measure changes in skin blood flow by Thomson[9] during the induction of anaesthesia. His results show that a significant increase in the apparent skin blood flow was induced by thiopentone, halothane or cyclopropane. However, this author did not give information on the time course of the changes during anaesthesia.

In the present study, the use of the thermal clearance method allows early detection of increases in skin blood flow. This increase results from a decrease in the vascular sympathetic tone induced by anaesthetic drugs. The change precedes the drop in blood pressure, suggesting a causal relationship between these two phenomena. Total body skin flow ranges from about 210 ml/minute in the cold to 8 litre/minute during maximal heating.[7] Therefore, increases in skin flow can cause the decrease in mean arterial pressure. Indeed, it is known that vasodilatation of splanchnic vessels occurs simultaneously with the increase in skin flow and both phenomena are responsible for hypotension.

A good baroreflex response to the decrease in

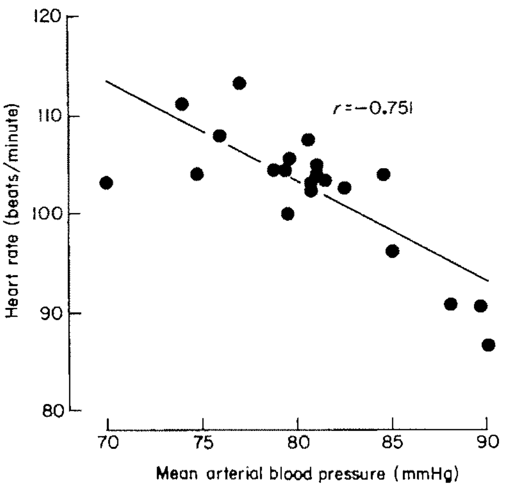


Fig. 2. Mean values of mean arterial blood pressure and heart rate were negatively correlated during the 20 minutes of anaesthesia.

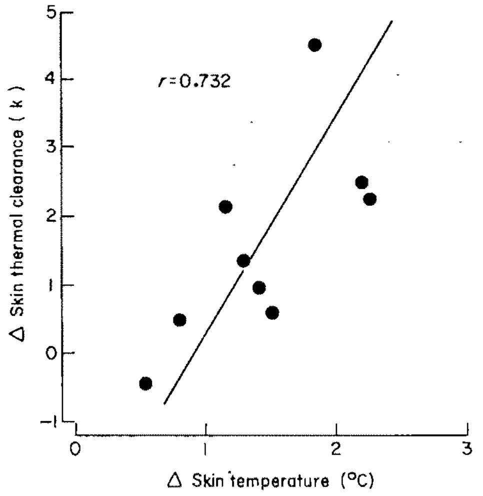


Fig. 3. Relationship between maximal changes in skin thermal clearance and skin temperature.

blood pressure occurred in our patients since the increase in heart rate correlated with the decrease in mean pressure. The increase in skin blood flow was responsible for an increase in skin temperature since the ambient temperature was constant. Maximal changes in skin thermal clearance and in skin temperature were correlated; skin thermometry has often been used to evaluate skin flow. Our results show that changes in thermal clearance occurred significantly before the increase in skin temperature. The thermal probe appeared to be a better device than skin thermometry for monitoring skin flow and for detecting small changes in vascular sympathetic tone during general anaesthesia.

References

1. Dittmar A, Marichy J, Grippari JL, Delhomme G, Roussel B. Measurement by heat clearance of skin blood flow of healthy, burned and grafted skin. In: Gautherie, M. and Albert, E., eds. *Biomedical thermology*. New York: (*Progress in Clinical and Biological Research Vol. 107*) A.R. Liss Inc. 1982: 413–9.
2. Detry JMR, Brengelmann GL, Rowell LB, Wyss C. Skin and muscle components of forearm blood flow in directly heated resting man. *Journal of Applied Physiology* 1972; **32:** 506–11.
3. Edholm OG, Fox RH, Macpherson RK. The effect of body heating on the circulation in skin and muscle. *Journal of Physiology* (Lond.) 1956; **134:** 612–9.
4. Challoner AV. Accurate measurement of skin blood flow by a thermal conductance method. *Medical and Biological Engineering* 1975; **13:** 196–201.
5. Cunningham DJ. An evaluation of heat transfer through the skin in the human extremity. In: Physiological and behavioral temperature regulation. Hardy JD, Gagge AP, Stolwijk JAJ, eds. Springfield, Ill: Charles C. Thomas, p. 302–11.
6. Degoute CS, Saumet JL, Banssillon V, Dittmar A. Skin blood flow measured by thermal clearance method in anesthesia. *Anesthesia and Analgesia* 1985; **64:** 179–80.
7. Levy L, Graichen H, Stolwijk JAJ, Calabresi M. Evaluation of local tissue blood flow by continuous direct measurement of thermal conductivity. *Journal of Applied Physiology* 1967; **22:** 1026–9.
8. Lipkin M, Hardy JM. Measurement of some thermal properties of human tissues. *Journal of Applied Physiology* 1954; **7:** 212–7.
9. Thompson WJ. The effect of induction of anaesthesia on peripheral haemodynamics. *British Journal of Anaesthesia* 1967; **39:** 210–4.

Anaesthesia, 1986, Volume 41, pages 390–394

The effect of halothane on cerebral electrical activity

An assessment using the cerebral function analysing monitor (CFAM)

KATHRYN J. WARK, P. S. SEBEL, C. VERGHESE, D. E. MAYNARD AND S. J. W. EVANS

Summary

Recordings of cerebral electrical activity were obtained using the cerebral function analysing monitor from eight unpremedicated patients anaesthetised with increasing concentrations of halothane in oxygen. The amplitude of the processed EEG increased at one and decreased at two minimal alveolar concentrations. The frequency distribution of the weighted EEG signal showed a linear increase of delta activity with a corresponding decrease in beta activity with increasing concentrations of halothane.

Key words

Monitoring; electroencephalography.

The cerebral function analysing monitor (CFAM)[1,2] is a microprocessor based development of the cerebral function monitor.[3] It provides a continuous detailed analysis of amplitude trends and frequency distribution of the weighted electroencephalographic (EEG) signal derived from a single pair of surface electrodes.

A previous study with the CFAM in patients anaesthetised with thiopentone, nitrous oxide, oxygen, halothane,[2] demonstrated that anaesthesia was associated with a gradual decrease in weighted EEG amplitude and an increase in lower frequency activity. When nitrous oxide was stopped, there was an immediate steep rise in weighted EEG amplitude, accompanied by activity in the higher frequency bands. Nitrous oxide used alone in healthy volunteers[4] produces a decrease in amplitude, with no consistent or specific frequency changes. This study was designed to assess the effects of increasing concentrations of halothane, used alone, on cerebral electrical activity.

Methods

Following local Ethical Committee approval, eight consenting unpremedicated patients (ASA I), six female, two male, mean age 36.3 (SD 4.0) years were studied. The recording electrodes used were silver/silver chloride dome electrodes, attached to the scalp with collodion, and electroconductive jelly inserted under the dome after abrading the scalp. The biparietal position was chosen in this study, as this area normally has high amplitude EEG (minimising the signal to noise ratio), is least affected by scalp muscle activity, is relatively free from eye movement artefacts and is not easily disturbed by anaesthetic manipulations. CFAM recording was com-

---

Kathryn J. Wark, MB BS, FFARCS, Senior Registrar, Department of Anaesthetics, P.S. Sebel, MB, BS, PhD, FFARCSI, Senior Lecturer and Honorary Consultant, C. Verghese, MB, BS, FFARCS, Lecturer and Honorary Senior Registrar, Anaesthetics Unit, D.E. Maynard, MPhil, PhD, Principal Scientific Officer, Department of Clinical Neurophysiology, S.J.W. Evans, MSc, Senior Lecturer, Department of Clinical Epidemiology, The London Hospital and London Hospital Medical College, Whitechapel, London E1 1BB.

0003–2409/86/040390 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

menced 5 minutes prior to induction, with the patient awake and breathing air. Each subject was fully monitored with regular recordings of blood pressure, pulse rate and respiratory rate and temperature using a Datascope BP monitor and ECG. Anaesthesia was then induced with oxygen and halothane and continued, following suxamethonium and tracheal intubation, using intermittent positive pressure ventilation with a Manley Ventilator. The patients were maintained for 15 minutes sequentially at concentrations of one, and then two, minimal alveolar concentrations (MAC) (0.7 percent and 1.5 percent) end-tidal halothane in oxygen, measured using an Engstrom Emma. Ventilation was adjusted to maintain an end-tidal carbon dioxide (measured with a Gould Godart Mk II capnograph) of 4–5 percent. A continuous CFAM recording was made 5 minutes prior to induction, 15 minutes at each MAC. The CFAM data were transmitted at 1-minute intervals to magnetic tape for off-line analysis. Data are presented as mean (SEM) and statistical analyses were with one way repeated measures analysis of variance (BMDP2V) with orthogonal decomposition. This method makes proper allowance for the fact that observations at different times are made on the same subjects (hence, repeated measures). Orthogonal decomposition of ANOVA is able to assess linear and curvilinear trends over time. The frequency data were analysed as the logarithm of the delta/beta ratio. The logarithm of the ratio was used because ratios have a positively skew distribution whereas their logarithms are more symmetrical.

Results

The CFAM trace from one subject is shown in Fig. 1. The trace is representative of recordings from all subjects and shows an increase in amplitude at 1MAC and a decrease at 2MAC, which did not return to pre-induction values during the period of this study.

Pooled minute mean data from the digital tape recordings of CFAM amplitude and frequency from all subjects for the pre-induction period, and the first and last 5 minutes of 1MAC and 2MAC were used for statistical analyses (Table 1). In two subjects, the study was discontinued at 2MAC halothane because the systolic blood pressure fell below 80 mmHg. There was a statistically significant change with time in mean amplitude. This increased at 1MAC and decreased at 2MAC. Analysis of data from 10th and 90th centiles of the EEG amplitude showed similar results.

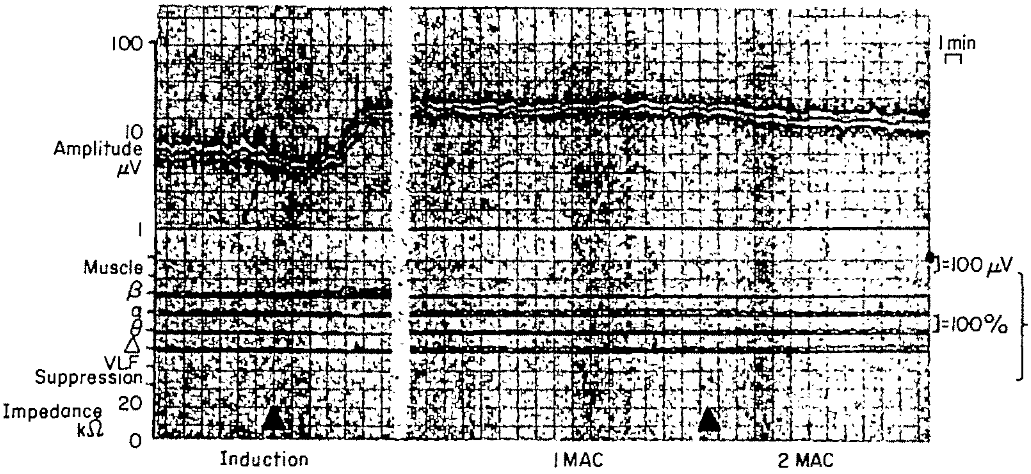


Fig. 1. Trace of the CFAM from one of the patients studied. The top line is the time marked in minutes. The amplitude tracing shows the 90th centile, mean and 10th centile. The lower half of the tracing shows, going down, muscle activity, beta, alpha, theta and delta band activity (each expressed as a percentage activity) very low frequency activity, burst suppression and impedance. The weighted EEG amplitude increased at 1 MAC and decreased at 2MAC but did not return to pre-induction levels. The frequency distribution showed an increase in delta and theta activity and a decrease in beta and alpha activity with increasing concentrations of halothane.

Table 1. Amplitude changes with halothane

	Mean amplitude	SEM
Pre-induction	58.9	(3.37)
First 5 minutes 1MAC	69.4	(2.94)
Last 5 minutes 1MAC	71.2	(2.71)
First 5 minutes 2MAC	64.0	(2.80)
Last 5 minutes 2MAC	63.6	(2.69)

$F = 7.61$; $p < 0.007$.

Table 2. Frequency changes with halothane

	$\text{Log}\,\frac{\text{delta}}{\text{beta}}$	SEM
Pre-induction	−0.517	(0.180)
First 5 minutes 1MAC	0.067	(0.255)
Last 5 minutes 1MAC	0.028	(0.245)
First 5 minutes 2MAC	0.346	(0.266)
Last 5 minutes 2MAC	0.500	(0.212)

$F = 3.81$; $p < 0.018$.

Visual analyses of the frequency data (Fig. 1) as displayed on the CFAM traces of all subjects, showed a progressive decrease in beta activity with a progressive increase in delta activity with increasing concentrations of halothane. These data (Table 2) were analysed at the same time points as the amplitude data using the logarithm of the ratio of delta to beta bands. The most significant term in the orthogonal decomposition was the first order (linear) term ($F = 8.68$; $p < 0.03$), indicating that the change was linear, i.e. with increasing concentrations, the amount of delta band activity increased and the amount of beta activity decreased. With increasing concentration of halothane, log delta to beta ratio increased from −0.517 (delta one third of beta) pre-induction to +0.500 (delta three times beta) at 2MAC (Table 2). There is a rise in this value at the first 5 minutes of 1MAC. If alpha and beta activity are summed and compared with the sum of delta and theta activity, then similar results are obtained.

Discussion

The usefulness of the EEG as an intra-operative monitor has been debated since the report by Gibbs and colleagues in 1937, of the occurrence of EEG changes during the administration of general anaesthetics.[5] EEG monitoring (using either the raw signal or some kind of processed EEG) has been recommended as useful for cerebrovascular surgery,[6] cardiopulmonary bypass,[7,8] deliberate hypotension and a measure of anaesthetic depth.[9,10] However, practical considerations, such as the size and complexity of the equipment, the need for a technician and the difficulty of making intra-operative interpretations of the EEG, have limited the popularity of the EEG as an intra-operative monitor.[11]

Monitoring depth of anaesthesia using the EEG has been relatively unsuccessful. Early work in this area concentrated on the EEG changes resulting from large variations in anaesthetic concentrations.[12,13] The widespread use of muscle relaxants and much lighter levels of anaesthesia has largely changed this picture, and the usefulness of the EEG in identifying small changes in anaesthetic depth is very limited.[14,15] There have been numerous reports describing relationships between the processed EEG and anaesthetics.[9,10,16,17] These suggest that information contained in the EEG may be sufficient to identify even small changes in anaesthetic depth, but that these changes are too small to be identifiable by routine analytical techniques, i.e. visual inspection. Only through automated analyses can these changes be identified and displayed for clinical use.

Various techniques of automated EEG analyses have been described in recent years. These include CFM and CFAM, which are commercially available. Power spectrum analyses are being studied now, in more detail.[18,19] All require special purpose electronic equipment not generally available. The CFM represents one extreme of the spectrum of devices that process the EEG, compressing all of the frequency and amplitude information in the EEG into a single tracing.[3]

The CFAM produces a detailed plot of amplitude trends and separate traces of the percentage activity in each of the classical EEG frequency bands. Its clinical application has been studied during intravenous anaesthesia and has been shown to be useful in monitoring depth of anaesthesia.[20] It has also been used during general anaesthesia with thiopentone, nitrous oxide, oxygen and halothane.[2] During maintenance of anaesthesia with patients breathing 2 percent halothane, there was a gradual decrease in EEG amplitude and a shift towards slower frequency EEG activity. Discontinuation of nitrous oxide resulted in a marked increase in EEG amplitude and an increase in alpha and beta band activity.

Discontinuation of halothane resulted in smaller alterations in the CFAM trace.

The results of a CFAM study[4] using nitrous oxide in increasing concentrations with healthy volunteers has shown that there was a gradual decrease in the EEG amplitude with increasing concentrations, and on discontinuation of the nitrous oxide there was a sharp rise in amplitude, demonstrating that the changes seen in the previous study were due to nitrous oxide. There were inconsistent and unreliable changes in the frequency bands.

In this study there was a shift in the amplitude with increasing concentrations of halothane, with an increase at 1MAC followed by a decrease at 2MAC. That the changes are not more marked during halothane anaesthesia is probably a result of the method of processing used, as the bands are filtered to attenuate the very low frequency activity (<1Hz). The frequency data were analysed using the logarithm of the ratio of beta to delta activity. The ratio initially showed a rise, i.e. an increase in beta activity relative to delta. This is interpreted as a deepening level of anaesthesia, as the patient often required a large inspired concentration of halothane for induction of anaesthesia. This was followed by a statistically significant increase in the ratio, i.e. an increase in the slower frequency or delta band activity, with a corresponding decrease in the faster or beta band activity. There was a wide variation in these results, as shown by the standard errors. Therefore, of the changes in the initial study with a general anaesthetic,[2] the amplitude changes are largely due to nitrous oxide, and this present study demonstrates that the frequency changes are due to halothane.

The changes that we have shown with halothane on the CFAM correspond to the EEG changes as described by Stockard and Bickford.[21] They showed that with increasing MAC values of halothane, there was a shift of power to the delta band. At 4MAC, almost all power is contained in 0.5Hz, 250 μV delta waves (even with normocapnia and normotension). This concentration was reached in only one patient; the ceiling for most of the other patients was 2–3 MAC, due to the hypotensive effect of the agent. This is also reflected in our results.

The Engstrom Emma was used to monitor the end-tidal halothane concentration. When compared with a laboratory interferometer, the EMMA was linear between 0.2 percent and 4.5 percent for all carrier gases, and there was a correlation coefficient of 0.999.[22] Water vapour produced increasing cross-sensitivity as a function of temperature.[23,24] In this study, the body temperature remained constant to within 0.5°C and the water vapour content was not thought to be a problem as we were using a Manley ventilator and a non-rebreathing system for a relatively short procedure.

The effect of suxamethonium on the EEG pattern has been described as either low voltage fast waves or high voltage slow waves, shown in children and adults.[25] They appeared several seconds after the appearance of muscle fasciculations and returned to the prestimulation pattern within 5–10 minutes if no further stimulation was applied. Low voltage fast (LVF) waves appeared in the older patients. The effects of suxamethonium would have worn off before we achieved stability at 1MAC halothane.

We have shown that changes in processed EEG, as measured by the CFAM, are consistent during halothane anaesthesia. The CFAM therefore represents an advance over the CFM in giving both amplitude and frequency information. Whether it will be useful as a clinical tool for monitoring anaesthesia requires further investigation.

References

1. Maynard DE, Jenkinson JL. The cerebral function analysing monitor: initial clinical experience, application and further development. *Anaesthesia* 1984; **39:** 678–90.
2. Sebel PS, Maynard DE, Major E, Frank M. The cerebral function analysing monitor (CFAM)—A new microprocessor-based device for the on-line analysis of the EEG and evoked potentials. *British Journal of Anaesthesia* 1983; **55:** 1265–70.
3. Maynard DE, Prior PF, Scott DF. Device for continuous monitoring of cerebral activity in resuscitated patients. *British Medical Journal* 1969; **4:** 545–6.
4. Williams DJM, Morgan RJM, Sebel PS, Maynard DE. The effect of nitrous oxide on cerebral electrical activity. *Anaesthesia* 1984; **39:** 422–5.
5. Gibbs FA, Gillis EL, Lennox WG. Effect on the electro-encephalogram of certain drugs which influence nervous activity. *Archives of Internal Medicine* 1937; **60:** 154–66.
6. Sharbrough FW, Messick JM Jr, Sundt TM Jr. Correlation of continuous electroencephalograms with cerebral blood flow measurements during carotid endarterectomy. *Stroke* 1973; **4:** 674–83.
7. Kritikou PE, Branthwaite MA. Significance of changes in cerebral electrical activity at onset of

cardiopulmonary bypass. *Thorax* 1977; **32:** 534–8.

8. Thomas WA, Cole PV, Etherington NJ, Prior PF, Stefonsson SB. Electrical activity of the cerebral cortex during induced hypotension in man. *British Journal of Anaesthesia* 1985; **57:** 134–41.
9. Prior PF, Maynard DE, Brierly JB. EEG monitoring for the control of anaesthesia produced by the infusion of Althesin in primates. *British Journal of Anaesthesia* 1978; **50:** 993–1000.
10. Dubois M, Savege TM, O'Carroll TM, Frank M. General anaesthesia and changes on the cerebral function monitor. *Anaesthesia* 1978; **33:** 157–64.
11. Levy WJ, Shapiro HM, Maruchak G, Meathe E. Automated EEG processing for intraoperative monitoring. *Anesthesiology* 1980; **53:** 223–36.
12. Bickford RG. Automatic electroencephalographic control of general anesthesia. *Electroencephalogy and Clinical Neurophysiology* 1950; **2:** 93–6.
13. Verzeano M. Servo-motor integration of the electrical activity of the brain and its applications to the automatic control of narcosis. *Electroencephalogy and Clinical Neurophysiology* 1951; **3:** 25–30.
14. Robson JG. Measurement of depth of anaesthesia. *British Journal of Anaesthesia* 1969; **41:** 785–8.
15. Clark DL, Hosick EC, Rosner BS. Neurophysiological effects of different anesthetics in unconscious man. *Journal of Applied Physiology* 1971; **31:** 884–91.
16. Findeiss JC, Kien GA, Huse KOW, Linde HW. Power spectral density of the electroencephalogram during halothane and cyclopropane anesthesia in man. *Anesthesia and Analgesia* (Cleve) 1969; **48:** 1018–23.
17. Bart DJ, Homi J, Linde HW. Changes in power spectra of electroencephalograms during anesth with fluroxene, methoxyflurane and ethrane. *A thesia and Analgesia* (Cleve) 1971; **50:** 53–63.
18. Berezowsky JL, McEwen JA, Anderson Jenkins LC. A study of anaesthesia depth by po spectral analysis of the electroencephalog (EEG). *Canadian Anaesthetists' Society Jou* 1976; **23:** 1–8.
19. Rampil IJ, Sasse FJ, Smith NT, Hoff Flemming DC. Spectral edge frequency—a correlate of anesthetic depth. *Anesthesiology* 1 **53:** (suppl.) S12.
20. Frank M, Maynard DE, Tsanaclis LM, Ma E, Coutinho P. Changes in cerebral electr activity measured by the cerebral function ana ing monitor following bolus injections of t pentone. *British Journal of Anaesthesia* 1984; 1075–81.
21. Stockard J, Bickford R. The neurophysiolog anaesthesia. In: Gordon, E. ed. *A basis and prac of neuroanaesthesia.* Monographs in an thesiology Volume II. Amsterdam: Exce Medica, 3–46.
22. Kay B, Cohen AT, Wheeler MF. A laborat investigation of a multigas monitor for anaesth (EMMA). *Anaesthesia* 1982; **37:** 446–50.
23. Linstromberg JW, Muir JJ. Cross-sensitivit water vapour in the Engström EMMA. *Anesth and Analgesia* 1984; **63:** 75–8.
24. Hayes JK, Westenskow DR, Jordan Continuous monitoring of inspiratory and e tidal anesthetic vapor using a piezoelectric detec *Anesthesiology* 1982; **57:** A180.
25. Oshima E, Shingu K, Mori K. EEG activity du halothane anaesthesia in man. *British Journa Anaesthesia* 1981; **53:** 65–72.

Anaesthesia, 1986, Volume 41, pages 395–397

CASE REPORT

Anaesthesia for congenital analgesia

A case report

P. R. LAYMAN

Summary

Bilateral amputations were performed without analgesia on a patient with congenital insensivitivity to pain (congenital analgesia). Positioning, vasomotor control and possible sensitivity to anaesthetic drugs are discussed.

Key words

Analgesia; congenital.

Congenital insensitivity to pain (congenital analgesia or hereditary sensory and autonomic neuropathy) is a rare condition that, despite the apparent paradox, requires anaesthetic management. This case report discusses some points that are applicable both to this case and to the more common sensory neuropathies.

Case history

I.P. was 33-years-old when he appeared on an orthopaedic surgery list for bilateral amputation. He had first presented at the age of 2 years with marked bowing of his legs, several septic spots and a raw right thumb which he chewed. At the age of 5 years he was noted to have ulcerating lesions of his hands and feet and several healing bony lesions of different ages. The diagnoses of osteodystrophy or congenital insensitivity to pain were suggested and by the age of 7 years it was clear that he had congenital analgesia.

At the age of 13 years he had developed the destructive arthropathy of Charcot in both ankles and his left knee, which was later ankylosed to improve stability of his leg. At the age of 16 years his mobility was very poor. He could move around the house by himself but needed a wheelchair outside. He continued to have indolent ulcers of his heel, ankles and fingers. During this time, blood tests and injections were painless although he could feel the passage of the needle through the skin. His fingers deteriorated to such an extent that amputation of several of them was necessary and was performed without anaesthetic, although diazepam was used for sedation. A year later he burnt what was left of his right index finger while smoking.

He was noted to be wheelchair bound at preoperative assessment, and had nicotine-stained stumps where his fingers had been removed. The feet were swollen and severely ulcerated. He had no fear of needles, and was looking forward to the operation as a way of improving his mobility. He was shown to have absence of pinprick sensation distal to the groins and axillae on both sides. There appeared to be normal sensitivity on the trunk and the tendon reflexes that could be tested were preserved. Blood pressure and pulse were

---

P.R. Layman, MB, ChB, FFARCS, Senior Registrar, Nuffield Department of Anaesthetics, John Radcliffe Hospital, Oxford.

0003–2409/86/040395 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

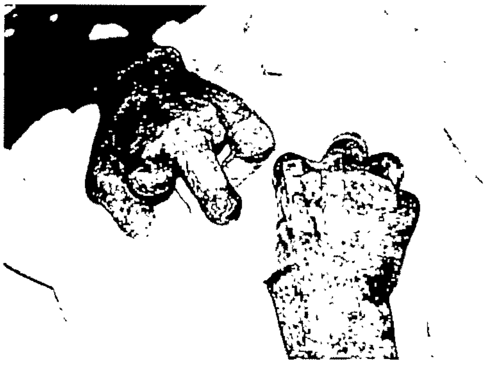


Fig. 1. Deformed hand following loss of fingers.

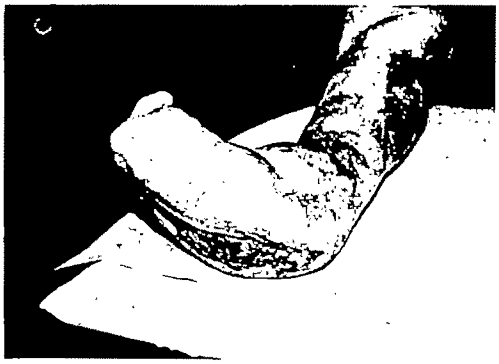


Fig. 2. Huge indolent ulcer on sole of foot.

within normal range as was the electrocardiogram and chest radiograph. Haemoglobin was 13.1 g/dlitre and Wasserman reaction was negative.

Anaesthesia

After discussion with the patient and the surgeons, it was decided to perform the amputations under sedation, as this had proved successful for the finger amputations, and was less likely to cause cardiovascular instability, although there were no overt signs of loss of vasomotor control. Tourniquets on each thigh would be used to minimise blood loss. Temazepam 10 mg was given 1 hour pre-operatively.

He was positioned carefully on a sheepskin on the operating table with adequate padding for the arms. He was given oxygen at 4 litre/minute to breathe via a Hudson's mask, and a large intravenous cannula (14-gauge) was placed without anaesthetic and without pain in his forearm. Blood pressure and pulse were monitored frequently and the electrocardiogram was displayed. Midazolam was given intravenously in increments of 2 mg (to a total of 20 mg) to maintain adequate sedation, and thiopentone was given in 50 mg increments totalling 700 mg over the 3 mg increments totalling 700 mg over the 3-hour operation. No analgesics were needed. There was no cardiovascular response to skin incision or division of the bones. Clamping of the nerve trunks in the popliteal fossa, however, produced a flexion response lasting a few seconds but caused no apparent distress, except to the surgeons.

The operation otherwise proceeded uneventfully. He had amnesia for the entire surgical procedure. His wounds healed well and he was discharged 4 weeks later.

Discussion

The anaesthetist is more likely to meet varying degrees of acquired insensitivity to pain rather than the rare congenital types. Examples of the acquired variety are seen in diabetes, tabes dorsalis, the neuropathic form of leprosy, hemisection of the spinal cord (Brown-Séquard syndrome—unilateral loss of pain and temperature sensation) and syringomyelia (bilateral loss of pain and temperature sensation in the upper limbs). In addition, a large number of drugs can cause a peripheral neuropathy.[1]

The group of patients with congenital insensitivity to pain can be subdivided according to their vasomotor instability, absence of sweating and other neurological features.[2-4] Our patient had insensitivity to pain, but apparently normal sensitivity to tactile stimuli, with preserved tendon reflexes, muscle power, and no loss of vasomotor control. Some may have total absence of pain, others such as our patient, may have distal loss with islands of normal sensation.

The mechanism of congenital insensitivity to pain is not well understood. Total absence of pain sensation has been produced experimentally in newborn rats by the use of the drug capsaicin, which destroys small unmyelinated nerve fibres.[5] Sural nerve biopsies in human patients with hereditary insensitivity to pain also show a diminution in the number of small fibres, but this does not exclude the possibility of non-functioning nociceptors or a central insensitivity to pain.[2,6] Endogenous opiates have been implicated as a possible explanation and naloxone has been shown to have a pain-restoring effect in one patient, but to have no effect in others.[7]

For many years, our patient showed the destruction that occurs when undue pressure, which would otherwise be painful, is ignored. Management of the individual patient with some degree of insensitivity to pain, should take into account this susceptibility to pressure ulceration of the skin. Attention to careful positioning on the operating table and generous padding is necessary, and rapid emergence from anaesthesia may help to prevent postoperative pressure problems.

There is a tendency for vasomotor instability, especially in the variety of congenital analgesia called familial dysautonomia.[8] Prediction of this in other neuropathies is difficult, and the Valsalva manoeuvre as a test of sympathetic reflexes has been shown to be unreliable as a predictor of orthostatic hypotension.[10] Appropriate monitoring and measures to control the blood pressure should be available, and careful measurement of intra-operative blood loss is essential. The common indicators of depth of anaesthesia may not be valid and the patient with islands of normal sensation is likely to react briskly if surgical procedures encroach on the normal areas. Our patient did not show any of these problems.

There may be sensitivity to some drugs and a case of suxamethonium apnoea has been reported.[3,9] The possibility of postoperative respiratory inadequacy has to be considered as with other neurological diseases when long acting neuromuscular relaxants are used.

The general principles of the management of a case of insensitivity to pain have been discussed. In addition to being a medical curiosity, this group of conditions may help in the understanding of the complex physiology of acute and intractable pain.

Acknowledgments

I wish to thank Mr J. Spivey, consultant orthopaedic surgeon, for permission to report this case, and Miss P. Hammans for secretarial assistance.

References

1. Argov Z, Mastaglia FL. Drug induced peripheral neuropathies. *British Medical Journal* 1979; **1:** 663–6.
2. Dyck PJ, Mellinger JF, Reagan TJ, Horowitz SJ. Not 'indifference to pain' but varieties of hereditary sensory and autonomic neuropathy. *Brain* 1983; **106:** 373–90.
3. Verity CM, Dunn HG, Berry K. Children with reduced sensivitity to pain: assessment of hereditary sensory neuropathy types II and IV. *Developmental Medicine and Child Neurology* 1982; **24:** 785–97.
4. Anonymous. Insensitivity to pain. *British Medical Journal* 1973; **4:** 187–8.
5. Fitzgerald M. Capsaicin and sensory neurones —a review. *Pain* 1983; **15:** 109–30.
6. Casey KL. Toward a neurophysiology of pain. *Headache* 1969; **8:** 141–53.
7. Pasi A, Meyer M, Boltshauser E, Foletta D, Gramsch C. Failure of naloxone to reverse analgesia in congenital insensitivity to pain, and variable plasma levels of β-endorphin-like activity. *Lancet* 1982; **1:** 622.
8. Kadis LB. Familial dysautonomia. In: Katz J, Kadis LB, eds. *Anesthesia and uncommon diseases. Pathology surgical and clinical correlations.* Philadelphia: W.B. Saunders, 1981: 502–3.
9. Kawata K, Nishitateno K, Kemi C, Yanagida H. Anaesthetic considerations of congenital insensitivity to pain. *Japanese Journal of Anesthesiology* 1975; **50:** 820–24.
10. Rawlinson WAL, Edmonds-Seal J, Adams AP. Anaesthesia and the Valsalva manoeuvre. A test of circulatory responses in neurosurgical patients including those in the sitting position. *Anaesthesia* 1979; **34:** 534–42.

Anaesthesia, 1986, Volume 41, pages 398–400
CASE REPORT

Raynaud's phenomenon precipitated by blood transfusion

JULIA K. MOORE AND D. W. PROCTOR

Summary

A patient undergoing surgery with spinal anaesthesia received a transfusion of concentrated red cells. Whenever the rate of blood transfusion reached a certain critical value, the symptoms and signs of Raynaud's phenomenon appeared in the hand distal to the site of the intravenous cannula. Possible causes of this transfusion-induced vasospasm are discussed.

Key words

Transfusion; stored blood.
Complications; Raynaud's phenomenon.

Uncomplicated Raynaud's disease does not usually pose a problem for the anaesthetist. We report a case where blood transfusion precipitated intense vasospasm.

Case history

A 46-year-old female presented with severe unilateral osteoarthritis of the hip. She had been grossly overweight for years, but had managed to reduce her weight from twenty stones to twelve stones prior to total hip replacement. A non-smoker, she had an uneventful anaesthetic 7 years previously. On admission she was taking naproxen 500 mg twice daily and fenoprofen 400 mg as required for analgesia. History and clinical examination were unremarkable.

She was premedicated with papaveretum 15 mg and hyoscine 0.3 mg administered intramuscularly. Under local anaesthetic infiltration with 1 percent plain lignocaine 0.5 ml, an intravenous cannula (14-gauge) was introduced at the left wrist and an infusion of the warmed compound sodium lactate solution was commenced. A spinal anaesthetic was administered using 3.5 ml of 0.5 percent plain bupivacaine. This produced a bilateral sensory blockade to the level of T_6. One litre of compound sodium lactate solution was infused over the next 80 minutes, then, as blood loss increased, 500 ml of polygeline was infused over 20 minutes. This did not produce any symptoms or signs of histamine release. Blood transfusion was then commenced with filtered concentrated red cells and, after 100 ml had been delivered, a pressure infuser was used to speed the rate of delivery. Immediately, the patient complained of severe pain in the hand and fingers which, on inspection, were blanched with a clear demarcation line at the wrist. The transfusion rate was slowed and the fingers became cyanosed, then gradually returned to normal and the pain subsided. The radial pulse was palpable and unchanged throughout. This cycle was repeated each time the transfusion rate was increased, with

---

Julia K. Moore, MB, ChB, FFARCS, Senior Registrar in Anaesthesia, Royal Infirmary, Glasgow G31 1BR, D.W. Proctor, MB, ChB, FFARCS, DRCOG, Consultant Anaesthetist, Western Infirmary, Glasgow G11 6NT

0003–2409/86/040398 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

pain radiating into the forearm but no other systemic complaints. The blood warmer was functioning and the patient was closely monitored for signs of a generalised transfusion reaction, but none were noted. There was no positional restriction to the venous drainage of the limb and the sphygmomanometer cuff was on the other arm. A second unit of concentrated red cells produced the same effect. Both units of blood were viable for a further 11 days before expiry. Partial relief was afforded by the intravenous injection of 1 percent plain lignocaine 5 ml through the cannula, after exsanguination of the hand and forearm, but discomfort gradually recurred as transfusion was continued and the patient was then sedated with 2 mg of midazolam. A further two units of blood were transfused over 8 hours in the recovery ward. The patient's axillary temperature was 35.8°C on arrival in the recovery ward and rose to 36.8°C within the first 2 hours.

On direct questioning the patient described Raynaud's syndrome in her hands and feet over many years, usually following exposure to cold, which suggested Raynaud's phenomenon rather than any other cause of arterial vasospasm. She was reviewed 3 months postoperatively, when haematological and biochemical tests, serum immunoglobulins and serum protein electrophoresis were normal. Rheumatoid factor was negative. DNA binding capacity was normal and antinuclear factor was positive at 1/1000. There was no evidence of any other underlying disorder and she was simply advised to avoid exposure to cold.

Discussion

In the case described, localised Raynaud's phenomenon developed during the infusion of concentrated red cells above a critical flow rate, despite warming to body temperature, in a patient undergoing surgery with spinal anaesthesia.

Raynaud's syndrome has been defined as intermittent vasospasm of the arterioles of the distal limbs, often following exposure to cold or emotional stimuli. It may be associated with underlying diseases, notably scleroderma, or may occur alone when it is known as Raynaud's disease. True Raynaud's disease occurs mostly in young females and is most common in the upper limbs.[1] The aetiology is unknown, but overactivity of the sympathetic nervous system with excess production of neurotransmitter, or interference with the inactivation of noradrenaline have been postulated.[2] Pallor and cyanosis are precipitated by arterial vasoconstriction of the digital arteries with stasis of blood, followed by erythema and oedema when the arteries reopen. Numbness and pain often occur during the attacks and the ischaemic episode is followed by burning and throbbing pain.

Treatment is aimed at avoiding precipitant factors and abstinence from cigarette smoking. Arterial spasm may be relieved by intravenous reserpine[3] or guanethidine[4] into a tourniquet-isolated limb, and α-adrenergic antagonists have also proved useful.[5] Sympathetic blockade may be induced by stellate ganglion or lumbar sympathetic block and produces vasodilatation of the limb with symptomatic relief.[6]

There are no specific recommendations as to the choice of drugs to produce general anaesthesia. Maintenance of body temperature and the warming of infusion fluids is logical and a non-invasive technique is advisable for the measurement of blood pressure if possible. Regional anaesthesia has been recommended, but adrenaline should be avoided as prolonged vasoconstriction has been reported, with sensory deficits in the fingers lasting for 24 hours after axillary block with 1.5 percent lignocaine containing adrenaline 1:100 000.[7]

Pain and unilateral cyanosis have been reported following the injection of local anaesthetic around the wrist[8] and have also followed the intravenous injection of methohexitone[9] in a patient with scleroderma. In that report it was suggested that the tight skin may have impaired venous return with retrograde flow to small veins and capillaries, thus provoking vascular spasm. It is difficult to explain why our patient did not develop pain with the rapid infusion of crystalloid, but only with the infusion of concentrated red cells. An increase in viscosity of the blood, associated with a raised plasma fibrinogen concentration and increased red blood cell aggregation has been reported in Raynaud's disease,[10] and this may lead to sludging and slowing of blood flow. It may be that, once a critical transfusion rate was reached, the viscosity of the concentrated red cells was sufficient to alter flow characteristics in the arm; the resultant retrograde flow or stasis within the small vessels of the hand caused ischaemia and precipitated Raynaud's phenomenon. An agent specific to the transfused blood is unlikely, as no problems were encountered with the transfusion until the rate was increased, and the problem recurred with the second unit of blood. All transfused fluids were warmed to body temperature and a temperature provoked response is therefore unlikely.

Fortunately, our patient had received no sedation other than premedication and she was able to complain immediately. Had she been heavily sedated, or received a general anaesthetic, the ischaemia might not have been noticed; all four units, transfused rapidly, might have resulted in potentially serious sequelae.

Acknowledgments

We would like to thank Mr J. Graham, FRCS, Consultant Orthopaedic Surgeon, Western Infirmary, for his permission to report this case, and Dr J.H. Dagg, MD, FRCP, Consultant Physician, Western Infirmary, for his assessment of the patient postoperatively.

References

1. Weatherall DJ, Ledingham JGG, Warrell DA. *Oxford textbook of medicine*. Oxford. Oxford University Press, 1983: 291 (Ch 13).
2. Stoelting RK, Dierdorf SF. *Anesthesia and co-existing disease*. New York: Churchill Livingstone, 1983: 160–1.
3. Gorsky BH. Intravenous perfusion with reserpine for Raynaud's phenomenon. *Regional anesthesia* **2:** Vol. 5. Chicago, Illinois: J.B. Lippincott, 1977.
4. Holland AJC, Davis KH, Wallace DH. Sympathetic blockade of isolated limbs by intravenous guanethidine. *Canadian Anaesthetists' Society Journal* 1977; **24:** 597–602.
5. Gray TC, Nunn JF, Utting JE. *General anaesthesia*, 4th edn. London: Butterworth and Co., 1980: 755.
6. Atkinson RS, Rushman GB, Lee JA. A synopsis of anaesthesia, 9th edn. Bristol: John Wright and Sons, 1982: 643.
7. Eisele JH, Reitan JA. Scleroderma, Raynaud's phenomenon and local anesthetics. *Anesthesiology* 1971; **34:** 386–7.
8. Sweeney B. Anaesthesia and scleroderma. *Anaesthesia* 1984; **39:** 1145.
9. Davidson-Lamb RW, Finlayson MCK. Scleroderma. Complications encountered during dental anaesthesia. *Anaesthesia* 1977; **32:** 893–5.
10. Pringle R, Walder DN, Weaver JPA. Blood viscosity and Raynaud's disease. *Lancet* 1965; **1:** 1086–8.

Anaesthesia, 1986, Volume 41, pages 401–403
CASE REPORT

Accidental spinal anaesthesia following intrathoracic intercostal nerve blockade

A case report

M. R. J. SURY AND R. M. BINGHAM

Summary

A case of high spinal anaesthesia following intrathoracic intercostal nerve blockade is described and the possible causative mechanisms are discussed.

Key words

Anaesthetic techniques, regional; intercostal.
Complications; hypotension.

Spread of local anaesthetic agent from the site of injection has been described following a variety of local anaesthetic blocks and may unexpectedly result in serious complications.[1,2] We report one such complication, high spinal anaesthesia, following intrathoracic, intercostal nerve blockade, which has been hitherto unreported in the British literature.

Case history

A 66-year-old, 65-kg woman presented with a 10 week history of progressive hoarseness, associated with a dry cough. She was a non-smoker and otherwise asymptomatic. Nine years previously she had a sigmoid colectomy for a, stage Duke's A, colonic carcinoma and later that year she had another laparotomy for division of adhesions. There were no anaesthetic problems associated with either procedure. Routine physical examination was unremarkable, but indirect laryngoscopy revealed a left vocal cord paresis. A chest X ray showed a mediastinal mass close to the hilum of the right lung, but bronchoscopy was normal. Thoracic computerised tomography scan showed two masses, one posterior to the superior vena cava and the other subcarinal. These were felt to be inaccessible to mediastinoscopy and a thoracotomy was planned, to provide a tissue diagnosis.

Premedication of papaveretum 15 mg and hyoscine 0.3 mg was given one hour prior to introduction of anaesthesia with thiopentone 400 mg and papaveretum 4 mg. An 8-mm tracheal tube was passed with the aid of suxamethonium 75 mg and anaesthesia was maintained with 60 percent nitrous oxide in oxygen and 0.5 percent halothane. Her lungs were mechanically ventilated and neuromuscular blockade was maintained with a total of 10 mg alcuronium. The procedure lasted 90 minutes and blood loss was estimated at 400 ml. Before chest closure, intrathoracic intercostal nerve blocks were performed under direct vision at the angle of the 4th, 5th and 6th ribs, using a total of 10 ml of 0.5 percent bupivacaine with 1:200000 adrenaline. Shortly afterwards, the sys-

---

M.R.J. Sury, MB, FFARCS, Registrar, R.M. Bingham, MB, FFARCS, Senior Registrar, Department of Anaesthesia, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE.

0003–2409/86/040401 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

tolic arterial blood pressure fell to 60 mmHg from its previously stable level of 100 mmHg and the heart rate decreased from 70 to 60 beats/minute. The patient appeared peripherally vasodilated and an infusion of 1000 ml of gelatin solution restored the blood pressure to its previous value.

Postoperatively she seemed unduly slow to wake up and her pupils were noted to be dilated but reacting to light. She failed to resume spontaneous ventilation despite adequate reversal of neuromuscular blockade with 2.5 mg neostigmine. Confirmation of adequate reversal of neuromuscular blockade was made using a peripheral nerve stimulator. Following naloxone 0.4 mg she was able to open her eyes to command but otherwise did not move or breathe. At this stage, she was able to communicate with facial movements and it was established that she had no pain from the thoracotomy site. Pinprick sensation was absent, except in the distribution of the 5th cranial nerve. A diagnosis of high spinal anaesthesia was made and she was transferred to the intensive therapy unit awake, comfortable but still requiring artificial ventilation. Six hours later spontaneous respiratory efforts commenced and she was weaned easily from mechanical ventilation. She was found at this time to have no residual neurological impairment.

Discussion

There is little doubt that this patient had developed high spinal anaesthesia. Immediately following the intercostal nerve blocks, sympathetic paralysis was shown by vasodilatation, a reduction in heart rate and hypotension responding to colloid infusion. Postoperatively, there was complete loss of sensation and voluntary motor function below the distribution of the cranial nerves. Other possible explanations can be excluded. The narcotic effect of the anaesthetic and premedication was reversed with naloxone, and the neuromuscular blockade was adequately reversed, as shown by peripheral nerve stimulation. Intravenous injection of the bupivacaine would not cause incomplete paralysis of this distribution and an epidural injection of this volume of bupivacaine is unlikely to cause such profound effects. An injection of 10 ml of bupivacaine into the thoracic epidural space could just conceivably cause a similar clinical picture, but for this to have occurred in our patient the surgeon would need to inject the epidural space three times, next to the three thoracic intercostal nerves.

Accidental spinal anaesthesia has followed many local anaesthetic techniques,[1-3] and there have been four previous reports of total or high spinal anaesthesia following intrathoracic, intercostal nerve blockade in the world literature.[3-6] There are several explanations which may account for this phenomenon. It is possible that dural cuffs enclose the spinal nerves to beyond the intervertebral foramina between the vertebrae and these may be pierced, giving direct access to the cerebrospinal fluid.[7] Injection into the nerve tissue itself may lead to extrafascicular (epineural) or intrafascicular (endoneural) distribution of local anaesthetic.[8] Epineural injection results in a low pressure (25–60 mmHg) gradient for spread of local anaesthetic within the neural tissue and spread is poor. Endoneural injection, on the other hand, can result in large pressures (300–750 mmHg) and more extensive spread. Endoneural injections of rabbit sciatic nerves have been shown to spread to the spinal cord and this may have been the mechanism of spread of local anaesthetic in our patient. Other possible mechanisms include retrograde axonal transport and simple diffusion.

Spinal anaesthesia is not the only serious complication following intercostal nerve blockade. Hypotension has been reported and spread of local anaesthetic to the paravertebral space and consequent sympathetic blockade has been held responsible.[9] A case of respiratory failure was reported following intercostal nerve blockade due to paralysis of intercostal muscles in a respiratory cripple.[10] It is possible that spread of local anaesthetic to the thoracic spinal cord, as in our patient, may also have been responsible for these problems.

These cases illustrate that total or high spinal anaesthesia, with their accompanying profound respiratory and cardiovascular effects, may unexpectedly occur following intercostal and other peripheral nerve blocks. This further emphasises the necessity for the presence of full resuscitation equipment and a person experienced in its use when blocks of this nature are performed.

Acknowledgments

We are grateful to Miss Fiona Whimster for her secretarial services.

References

1. Adriani J, Parmley J, Ochsner A. Fatalities and complications after attempts at stellate ganglion block. *Surgery* 1952; **32:** 615–9.
2. Gay GR, Evans JA. Total spinal anesthesia following lumbar paravertebral block: a potentially lethal combination. *Anesthesia and Analgesia* 1971; **50:** 344–8.
3. Otto CW, Wall CL. Total spinal anesthesia: a rare complication of intrathoracic intercostal nerve block. *Annals of Thoracic Surgery* 1976; **22:** 289–92.
4. Gallo JA, Lebowitz PW, Battit GE, Brunner JMR. Complications of intercostal nerve blocks performed under direct vision during thoracotomy: a report of two cases. *Journal of Thoracic and Cardiovascular Surgery* 1983; **86:** 628–30.
5. Benumof JL, Semenza J. Total spinal anesthesia following intrathoracic intercostal nerve blocks. *Anesthesiology* 1975; **43:** 124–5.
6. Scholl W, Makowski HV. High spinal anaesthesia following intrathoracic intercostal nerve block. Report of a case. *Anaesthesist* 1977; **26:** 151–2.
7. Moore DC. Efocaine: complications following its use. *Western Journal of Surgery* 1953; **61:** 635–8.
8. Selander D, Sjöstrand J. Longitudinal spread of intraneurally injected local anaesthetic. An experimental study of the initial neural distribution following intraneural injections. *Acta Anaesthesiologica Scandinavica* 1978; **22:** 622–34.
9. Skretting P. Hypotension after intercostal nerve block during thoracotomy under general anaesthesia. *British Journal of Anaesthesia* 1981; **53:** 527–9.
10. Casey WF. Respiratory failure following intercostal nerve blockade. *Anaesthesia* 1984; **39:** 351–4.

Anaesthesia, 1986, Volume 41, pages 404–407
CASE REPORT

Carcinoid syndrome with myasthenia gravis

An unusual and interesting case

S. J. KEENS, M. J. DESMOND AND J. E. UTTING

Summary

The anaesthetic management of a patient suffering from carcinoid syndrome and myasthenia gravis is described including the successful treatment of a carcinoid attack with intravenous aprotonin. The differences between myasthenia gravis and the myasthenic (Eaton-Lambert) syndrome are considered and the rationale for the choice of vecuronium as the muscle relaxant is discussed.

Key words

Complications; myasthenia gravis, carcinoid syndrome.
Neuromuscular relaxants; vecuronium.

Secreting carcinoid tumours are rare and myasthenia gravis is uncommon, with an incidence in the general population of around 1 in 30 000.[1] The chances of anaesthetising a patient with both conditions must therefore be extremely remote. We report a case of a patient who had these two pathological conditions, since the combination presents several interesting problems to the anaesthetist.

Case history

A 79-year-old man was admitted with symptoms and signs of incomplete intestinal obstruction. Two years previously he had a laparotomy for the same condition and a tumour of the bowel, histologically found to be carcinoid, was resected. Twelve months after that he was again admitted, this time with a three-week history of increasing weakness in his legs, abdomen, and back, a two-week history of diplopia and facial weakness, and troublesome diarrhoea.

Laboratory investigations at that time showed a raised level of 5-hydroxy-indole-acetic acid (5HIAA) in the urine (138 μmol/24 hour; normal range 15–75 μmol/24 hours) indicating a secreting carcinoid tumour. In addition, a positive titre of acetylcholine receptor antibodies was present in the serum and electromyography demonstrated findings typical of myasthenia gravis, with 39 percent fade of a train-of-four responses at 2 Hz and a progressive decrement to under 50 percent of the initial amplitude on stimulation at 50 Hz for 128 stimuli. A muscle biopsy showed changes compatible with the diagnosis of myasthenia and there was short-lived improvement in muscle power following administration of edrophonium. A diagnosis of myasthenia gravis was made and the patient was given pyridostigmine 60 mg three times a day, combined with prednisolone and azathioprine. This resulted in good return of motor power.

S.J. Keens, BSc, MB ChB, FFARCS, Lecturer, M.J. Desmond, MB ChB, MRCP, FFARCS, Registrar, J.E. Utting, MA, MBBChir, FFARCS, Professor, University Department of Anaesthesia, 4th Floor, Royal Liverpool Hospital, Prescot Street, Liverpool, L69 3BX.

0003–2409/86/040404 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Before his latest admission (a year after the diagnosis of myasthenia had been made) there had been a 3-month history of colicky abdominal pains associated with diarrhoea and a 7-day history of postprandial vomiting. At first this was managed conservatively with oral fluids, resulting in some amelioration of his symptoms, but as soon as solids were re-introduced he again began to vomit. Nasogastric aspiration and intravenous fluids were started and, as all oral intake was discontinued, the pyridostigmine was given intramuscularly in a dose of 1 mg five times a day.

An ultrasound scan demonstrated the presence of a mass associated with the bowel, and it was decided to proceed to laparotomy. The last dose of pyridostigmine was given 10 hours before surgery.

Anaesthesia

Induction of anaesthesia was with droperidol (5 mg), fentanyl (150 μg), and thiopentone (75 mg + 50 mg). Muscle relaxation was obtained with vecuronium 2.4 mg (0.04 mg/kg), and tracheal intubation was performed after preliminary inflation with a mixture of nitrous oxide and oxygen and spraying the cords with lignocaine 4 percent (2 ml). Maintenance of anaesthesia was with nitrous oxide and oxygen, without any volatile adjuvant. An arterial line was inserted into the radial artery and surgery commenced.

Apart from a transient decrease immediately after induction of anaesthesia, the arterial blood pressure was well maintained until a steady fall occurred 40 minutes after induction (Fig. 1, upper trace). Peripheral cyanosis became marked and the face and extremities appeared cold, although no bronchospasm was detected. An hour after induction of anaesthesia the patient's blood pressure, despite infusion of Hartmann's solution 1 litre, was 70/40 mmHg with a pulse rate of 60 beats/minute. This fall appeared to be associated with handling of the bowel and mesentery which was covered with small tumour deposits. The rate of fluid infusion was not increased, but aprotonin 200 000 units, was given over 2–3 minutes. Ten minutes after this, the patient's colour had improved markedly and his blood pressure had risen to 130/60 mmHg (Fig. 1, upper trace).

There was no further period of hypotension; indeed, blood pressure continued to rise, and for the remainder of the operation (40 minutes) was between 160/70 mmHg and 170/80 mmHg. Further fluid was administered during this period, consisting of Hartmann's solution 500 ml, and, towards the end of surgery, blood to replace a measured blood loss of 800 ml. Urine production during the operation, which lasted

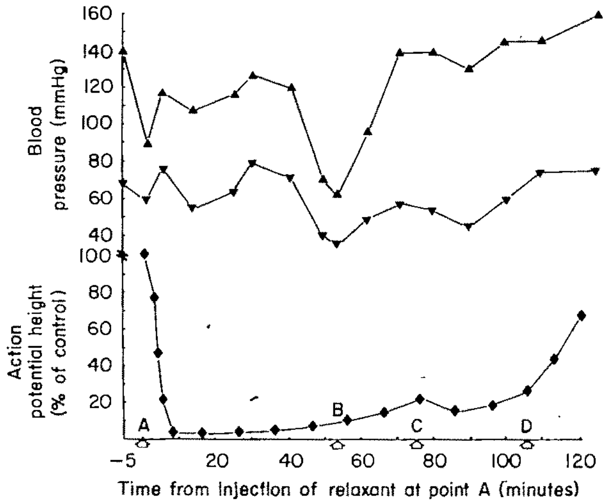


Fig. 1. Record of systolic and diastolic blood pressures (upper two traces) and of the percentage of the first action potential of the train-of-four to control (lower trace). A, induction of anaesthesia; B, the injection of aprotonin; C, an incremental dose of vecuronium; D, reversal of blockade with neostigmine.

1 hour 40 minutes, was 200 ml. As the tumour deposits were widespread and a recurrence was obstructing the small bowel, a bypass operation was performed as a palliative measure to relieve the obstruction.

Neuromuscular monitoring. Neuromuscular monitoring by electromyography during the procedure using the standard train-of-four pattern of stimulation, demonstrated that the initial dose of vecuronium administered (0.04 mg/kg) produced a decrease in the height of the first compound muscle action potential to 2.5 percent of control taken before giving the relaxant. Recovery from blockade was slow, taking 56 minutes to reach 10 percent and 73 minutes to reach 20 percent recovery, at which point a small increment of vecuronium (0.005 mg/kg) was administered (Fig. 1, lower trace). This was in contrast to the response of another patient with carcinoid syndrome, where vecuronium 0.1 mg/kg produced a decrease in height of the first action potential to 4.2 percent of control, and recovery to 10 percent took 15 minutes, whilst 20 percent recovery was reached at 24 minutes.

Reversal of neuromuscular blockade with neostigmine 5.0 mg (administered with atropine) was rapid and 7 minutes after the neostigmine the first action potential had reached 66 percent of control and the train-of-four ratio (ratio of the last action potential to the first) was 0.8. Spontaneous ventilation recommenced and recovery of consciousness was rapid when the nitrous oxide was discontinued. Anticholinesterase therapy was re-instituted 90 minutes after the neostigmine, when pyridostigmine 1 mg was given parenterally. One hour later, the first action potential had reached 94 percent of control and the train-of-four ratio was 0.98.

Discussion

This patient clearly had muscle weakness, although there were two possible types of myasthenia from which he might have been suffering: myasthenia gravis or the myasthenic (Eaton-Lambert) syndrome.

Typically, myasthenia gravis is found in young adult females. The history is usually one of progressive ptosis and blurring of vision, especially when tired. The weakness may involve any muscle but is often most severe in the ocular muscles. Edrophonium intravenously should produce a shortlived improvement in neuromuscular function—a test which may give some guide to the possible efficacy of regular anticholinesterase therapy. Acetylcholine receptor antibodies are often present in the serum and there is a progressive decrement in the amplitude of an evoked muscle action potential when the motor nerve is stimulated at a frequency of 50 Hz. In some patients there is an associated thymoma[2] (a postoperative CAT scan in the patient showed no thymic tumour).

Patients with the myasthenic syndrome, however, are usually in the older age group. The presentation is often one of weakness of the proximal muscle groups, associated with wasting. A carcinoma is almost invariably present and this is commonly bronchogenic. There is little or no improvement in neuromuscular function after injection of edrophonium and regular anticholinesterase therapy is rarely effective. Acetylcholine receptor antibodies are usually absent. There is often an increase in muscle strength with exercise and there is a progressive increase in the height of the evoked action potential when the motor nerve is stimulated at 50 Hz.[2]

This patient was suffering from myasthenia gravis, in view of the electromyographic findings, the presence of acetylcholine receptor antibodies and the positive response to edrophonium. Patients suffering from myasthenia gravis are sensitive to non-depolarising muscle relaxants, but may be resistant to suxamethonium,[3] or show early appearance of a dual block.[4] Patients with myasthenic syndrome, on the other hand, have an exaggerated response to both non-depolarising and depolarising muscle relaxants.[5] Despite the possibility of regurgitation during induction, suxamethonium was avoided because of this lack of predictability in myasthenia and because, in the carcinoid syndrome, an attack may be precipitated by the increased intra-abdominal tension brought about by the drug.[6] Pancuronium has been said to be the relaxant of choice for patients with carcinoid syndrome, because it is unlikely to provoke release of histamine or to cause hypotension.[7] This patient, however, had myasthenia gravis and therefore vecuronium, which is a shorter acting relaxant structurally related to pancuronium, was chosen, as this has been shown to be a satisfactory relaxant for operations on myasthenic patients[8] and does not readily release histamine.[9] To decrease the amount of relaxant required, the anticholinesterase therapy was withdrawn 10 hours pre-operatively and, although the patient was not distressed by his weakness, he required less than half the normal intubating dose of vecuronium (0.08–0.1 mg/kg); this dose lasted for considerably longer than would be expected in a normal patient.

Carcinoid tumours may secrete several different types of vaso-active substances, the predominant ones being either 5-hydroxytryptamine (5HT), or bradykinin. These substances are responsible for many of the symptoms. Serotonin produces diarrhoea, sedation and complex actions on the cardiovascular system which usually result in hypertension under general anaesthesia.[6] Bradykinin is thought to be involved in the classical carcinoid flush, and under anaesthesia often produces hypotension and bronchospasm.[6] Pre-operatively, the predominant symptom in this case was diarrhoea rather than flushing or bronchospasm and it was therefore assumed that this tumour secreted 5HT rather than bradykinin. However, the dramatic improvement in perfusion and blood pressure when aprotonin was given, suggests that bradykinin was involved in the episode of hypotension described above and supports the argument for having bradykinin antagonists available during surgery for carcinoid tumours, even if there is only evidence of serotonin secretion pre-operatively. Had there been any further cardiovascular instability during the operation, the patient would have been electively ventilated postoperatively. However, in view of the good condition at the end of surgery, neuromuscular block was reversed with a moderately large dose of neostigmine (with atropine) and the tracheal tube was removed. The postoperative course was uneventful and the patient was discharged home 2 weeks after the operation.

References

1. SCADDING EK, HAVARD CWH. Pathogenesis and treatment of myasthenia gravis. *British Medical Journal* 1981; **283:** 1008–12.
2. HENSON RA, URICH H. *Cancer and the nervous system: the neurological manifestations of systemic malignant disease*. Oxford: Blackwell Scientific Publications, 1982. Chapter 17, 420–1.
3. BARAKA A, AFIFI A, MUALLEN M, KACHACHI T, FRAYHA F. Neuromuscular effects of halothane, suxamethonium and tubocurarine in a myasthenic undergoing thymectomy. *British Journal of Anaesthesia* 1971; **43:** 91–5.
4. CHURCHILL-DAVIDSON HC. Abnormal response to muscle relaxants. *Proceedings of the Royal Society of Medicine* 1955; **48:** 621–4.
5. WISE RP. A myasthenic syndrome complicating bronchial carcinoma. *Anaesthesia* 1962; **17:** 488–504.
6. MASON RA, STEANE PA. Carcinoid syndrome: its relevance to the anaesthetist. *Anaesthesia* 1976; **31:** 228–42.
7. LIPPMANN M, CLEVELAND RJ. Anesthetic management of carcinoid patient undergoing tricuspid valve replacement. *Anesthesia and Analgesia, Current Researches* 1973; **52:** 768–71.
8. HUNTER JM, BELL CF, FLORENCE AM, JONES RS, UTTING JE. Vecuronium in the myasthenic patient. *Anaesthesia* 1985; **40:** 848–53.
9. BASTA SJ, SAVARESE JJ, ALI HH, SUNDER N, MOSS J, GIONFRIDDO M, EMBREE P. Vecuronium does not alter serum histamine within the clinical dose range. *Anesthesiology* 1983; **59:** A273.

Anaesthesia, 1986, Volume 41, pages 408–412

CASE REPORT

Multiple complications after internal jugular vein catheterisation

Z. GAMULIN, J.-C. BRÜCKNER, A. FORSTER, F. SIMONET AND J.-C. ROUGE

Summary

We report a case of a young female who developed multiple life threatening complications after a single internal jugular vein catheterisation. They consisted of pleural misplacement of the catheter, massive haemorrhage with cardiovascular collapse following catheter removal, and development of arteriovenous fistula, diagnosed 18 months later.

Key words

Complications; fistula, haemorrhage, misplacement.
Veins; cannulation, jugular.

Many different complications of central venous catheterisation have been documented,[1] but usually only one of them occurs per patient. We report the case of a patient who presented several successive severe complications following a single internal jugular catheterisation, which were not recognised immediately.

Case history

The patient was a 13-year-old girl weighing 29 kg, 140 cm tall, who was scheduled for surgical repair of multiple valvular disease. After induction of anaesthesia, the right internal jugular vein was punctured at the first attempt with a 14-gauge needle and a 16-gauge catheter (Intracath) was inserted through it without any difficulty by the first two authors. The puncture site was located between the two heads of the sternocleidomastoid muscle, 3 cm above the clavicle, as previously described.[2] The usual measures, such as aspiration of blood, adequate flow of infusion and gravitational blood reflux through the catheter, suggested correct intravenous placement. The catheter was connected via a three-way stopcock to an infusion line for drug administration and to a pressure transducer for intermittent measurement of central venous pressure.

Since the shape of the central venous pressure wave was not typical and the values were lower (0–1 mmHg) than those previously obtained during cardiac catheterisation (8 mmHg), pleural misplacement of the catheter was suspected. Nevertheless, blood reflux was still present when the catheter was aspirated. The persistence of blood clots in the operative field and the absence of change in activated clotting time (Haemochrom[3]) after the administration of 3 mg/kg of heparin through the internal jugular catheter, confirmed the misplacement of the catheter. The same dose of heparin was repeated through a peripheral venous catheter and the replacement of the aortic valve and the commissurotomy of the mitral and tricuspid valves

---

Z. Gamulin MD, J.-C. Brückner, MD, A. Forster, MD, J.-C. Rouge, MD, Department of Anesthesiology, F. Simonet, MD, Department of Surgery, University Hospital of Geneva, Switzerland.

0003–2409/86/040408 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

were performed uneventfully. At the end of the cardiopulmonary bypass, protamine was administered to restore the normalisation of activated clotting time (142 seconds).

Before the closure of the chest, surgical exploration of the right pleural cavity revealed the exact location of the catheter tip which was found floating in a small amount of blood. A right-sided chest tube was inserted but did not drain any blood, despite the application of continuous subatmospheric pressure. Because of the difficult access to the catheter sutured to the skin under sterile adhesive drapes, it was not removed until the end of surgery, after a postoperative chest X ray was taken (Fig. 1). Minutes later, while the patient was still in the operating room, the blood pressure decreased abruptly and dramatically and a blood loss of 2 litres was collected through the right chest tube to which subatmospheric pressure (15cmH$_2$O) was applied. The patient's haemodynamic status was rapidly corrected by massive transfusion, temporary external cardiac massage and continuous adrenaline infusion; the pleural aspiration was discontinued. The chest was immediately re-opened and the right pleural cavity reviewed. A small haemothorax and minimal bleeding through a small lesion at the dome of the pleura were discovered. This lesion was sutured, recovery was uneventful and the child was discharged from the hospital on the eleventh postoperative day.

Eighteen months later the patient was readmitted because of progressive congestive heart failure. Clinical examination revealed a right parasternal systolo-diastolic murmur. Catheterisation of the right side of the heart showed

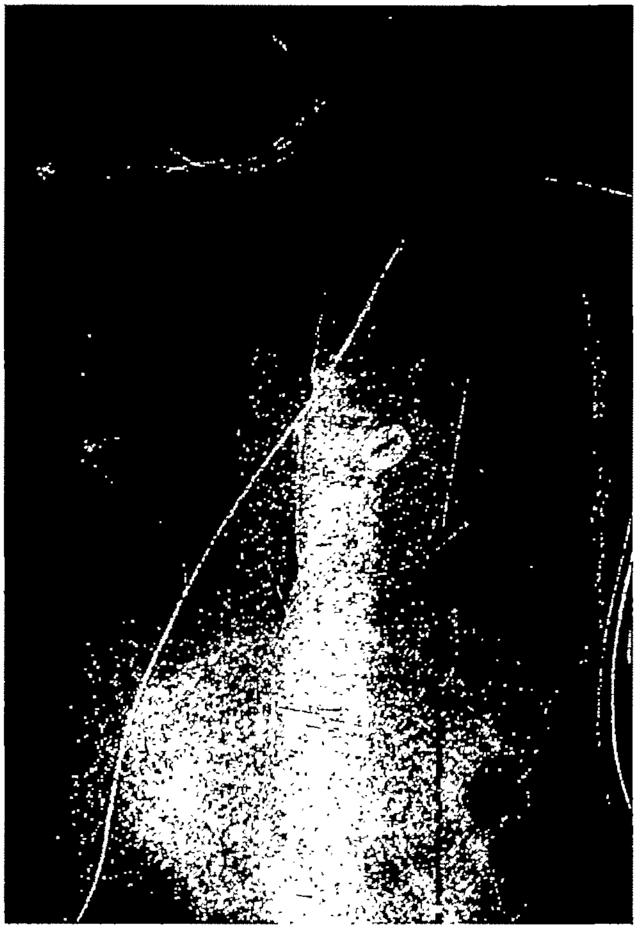


Fig. 1. Postoperative chest X ray before removal of the catheter.

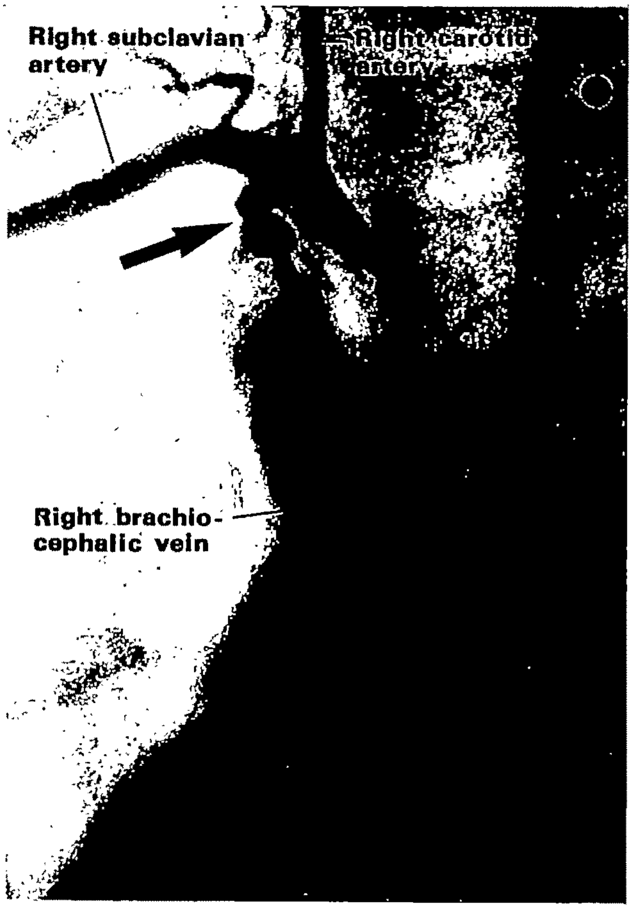


Fig. 2. Angiographic confirmation of the fistula (arrow) between the right subclavian artery and the right brachiocephalic vein.

a difference in oxygen saturation between samples of blood from the superior vena cava (74 percent) and the right atrium (66 percent). The presence of an arteriovenous fistula was therefore suspected and was confirmed by angiography. The fistula was located between the right subclavian artery and right brachiocephalic vein (Fig. 2) and its blood flow was considered significant by the cardiologist. Right and left ventriculography also revealed mitral and tricuspid insufficiency. The pressure in the right atrium was 22 mmHg, with a 'v' wave of 37 mmHg. During exploration of the chest at operation to replace the mitral valve and repair the tricuspid valve, a thrill was felt in the right brachiocephalic vein, which disappeared after ligation of a small channel (2.5 mm in diameter) located between the right subclavian artery and the posterior wall of the right brachiocephalic vein, near the junction of subclavian and internal jugular veins (Fig. 3). The ligation of the fistula was associated with an immediate decrease in central venous pressure from 22 mmHg to 15 mmHg.

Discussion

Several complications of internal jugular vein catheterisation are illustrated by this case: catheter misplacement, life threatening haemothorax and development of arteriovenous fistula.

Misplacement of the central venous catheter into the pleural cavity is a recognised complication and depends upon the puncture technique; it

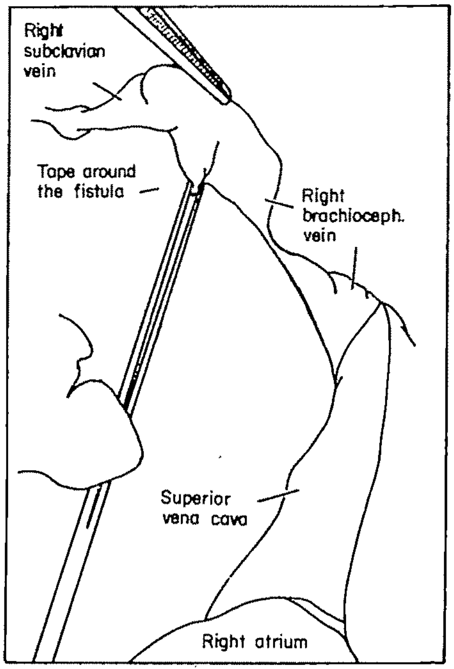


Fig. 3. Diagram drawn from photograph of operative site.

is rarely observed with the high internal jugular approach.[4] Its diagnosis can be easily missed.[5,6] In this case, the usual test to verify the intravascular position of the catheter was repeated several times and was misleading. The diagnosis of the misplacement was finally confirmed by the persistence of clots and normal activated clotting time despite the administration of a large dose of heparin through this catheter. A conventional chest X ray without contrast medium would probably not have been helpful in determining the position of the catheter accurately (Fig. 1). Rapid aspiration of a large quantity of blood through the catheter and/or comparison of the haematocrit of the refluxed blood with blood after rapid infusion of an isotonic solution obtained from another vessel, could have confirmed the diagnosis. If any doubt persists during open heart procedure, surgical exploration of the pleural cavity on the side of the puncture should be performed as soon as the chest is open.

The sudden massive intrapleural bleeding, which occurred immediately after the removal of the catheter, produced severe haemorrhagic shock, with a loss of 80 percent of the patient's blood volume (2 litres) in less than 5 minutes. This haemorrhage happened despite normal activated clotting time, was abrupt and was related to the removal of the catheter, since there were no haemothorax on the postoperative chest X ray (Fig. 1) and since no bleeding occurred through the right chest tube before the catheter was removed.

The application of a continuous negative pressure to the pleural cavity was probably responsible for the abruptness and magnitude of the bleeding and did not facilitate clotting because it maintained a high blood flow through the pleurovascular lesion. When the negative pressure was removed and blood volume restored, bleeding was minimal during the surgical re-intervention, and was easily controlled. This complication would probably have been less dramatic if the catheter had been removed immediately under direct vision of the pleural dome, and without negative pressure being applied to the pleural cavity.

This case should caution against the danger of puncturing subclavian or internal jugular veins in patients who have chest tubes under negative pressure on the same side. In addition, in rapidly developing haemothoraces induced by attempts at central venous catheterisation, application of negative pressure to the chest tube should be avoided, or performed only under close supervision. In our patient, bleeding could have been less dramatic if an over-the-needle catheter or Seldinger technique had been used instead of the through-the-needle catheter technique.

Arteriovenous fistula following central venous catheterisation has rarely been reported.[7,8] This complication is often not diagnosed because of its delayed appearance, even though it can produce a severe complication such as high output cardiac failure,[9] and possibly tricuspid insufficiency. In this case, right cardiac failure was related not only to the tricuspid insufficiency demonstrated by the cardiac catheterisation, but also to the iatrogenic arteriovenous fistula, since central venous pressure decreased by 7 mmHg when it was ligated.

In conclusion, this case suggests that delayed complications should be anticipated when any problem related to an internal jugular catheterisation occurs.

References

1. MORGAN RNW, MORRELL DF. Internal jugular catheterisation: a review of a potentially lethal hazard. *Anaesthesia* 1981; **36:** 512–7.

2. Civetta JM, Gabel JC, Gemer M. Internal-jugular-vein puncture with a margin of safety. *Anesthesiology* 1972; **36:** 622–3.
3. Hill JD, Dontigny L, De Leval M, Mielke CH Jr. A simple method of heparin management during prolonged extracorporeal circulation. *Annals of Thoracic Surgery* 1974; **17:** 129–34.
4. Rosen M, Latto IP, Ng WS. *Handbook of percutaneous central venous catheterization. The internal jugular vein.* Philadelphia: WB Saunders, 1981: 76–113.
5. Hopkinson RB, Parkin CE. Hydrohemothorax following percutaneous internal jugular vein cannulation recognized by intravenous pyelography. *Anesthesia and Analgesia* 1978; **57:** 507–11.
6. Mauritz W, Hertz H, Spiss CK, Sporn P. Infusionshydrothorax nach Katherisierung der Vena jugularis interna rechts. (Hydrothorax after catheterization of the right internal jugular vein). *Anaesthesie Intensivtherapie Notfallmedizin* 1981; **16:** 159–61.
7. Miguel Alonso JL, Rivero M, Vidal O, Montero Garcia A, Sanchez Sicilia L. Fistula arteriovenosa secundaria a punction de la vena subclavia por via infraclavicular. (Arteriovenous fistula caused by puncture of the subclavian vein by infraclavicular route.) *Revista Clinica Espanola* 1973; **130:** 353–6.
8. Farhat K, Nakhjavan FK, Cope C, Yazdanfar S, Fernandez J, Gooch A, Goldberg H. Iatrogenic arteriovenous fistula: a complication of percutaneous subclavian vein puncture. *Chest* 1975; **67:** 480–2.
9. Muenster JJ, Graettinger JS, Campbell JA. Correlation of clinical and hemodynamic findings in patients with systemic arteriovenous fistulas. *Circulation* 1959; **20:** 1079–86.

Anaesthesia, 1986, Volume 40, pages 413–418

APPARATUS

The digital control of anaesthetic gas flow

R. W. BOADEN AND P. HUTTON

Summary

The theory and construction of a prototype digital gas flow controller are described. Using eight preset needle valves, it has the ability to deliver any flow from 50 to 12750 ml/minute in steps of 50 ml/minute. Under given conditions, the accuracy of this device is very high and its variation in performance with pipeline supply pressures is quantified. The required flow is requested from a BBC 'B' microcomputer which is interfaced with the equipment via a program written in Basic and the 1MHz bus port. The possible uses and potential of a microcomputer-controlled flow regulator in anaesthesia and intensive care are discussed.

Key words

Equipment; anaesthetic machines, flowmeters

The incorporation of microprocessors into electronic systems is now commonplace, but in anaesthetic practice their use is almost exclusively limited to patient monitoring, where they enable sophisticated techniques to be used for the collection and display of physiological variables. There are, however, many other potential applications; time dependent drug infusions to maintain a constant serum level[1,2] and the control of ventilators are two obvious examples.

This paper describes the design and development of a digital gas flow regulator, which allows a microcomputer to control gas flow directly. Such a device has many uses because of the ease with which continually changing flow requirements and the possibility of feedback control from end-tidal $P\text{CO}_2$ can be accommodated by simple programming.

Principle of operation

The equipment is shown diagrammatically in Fig. 1 and, after construction, in Fig. 2. The high pressure gas enters the inlet manifold and is split into eight channels. Each channel can have the flow down it switched on or off by a miniature solenoid valve. When the solenoid valve is open, flow down any given channel is controlled by a preset needle valve. The eight needle valves are calibrated and locked in binary sequence, such that each one allows double the flow of the previous one. If the minimum flow is set at 50 ml/minute, then the maximum flow with all the valves open is 12750 ml/minute. Given the appropriate combination of valves open and closed, any flow between zero and the upper limit may be obtained in steps of 50 ml/minute, i.e. there is a rangeability of 255 to 1. The required valves are switched on or off when a given flow is requested

---

R.W. Boaden, BSc, MB, BS, FFARCS, Senior Registrar in Anaesthesia, P. Hutton, BSc, PhD, MB, ChB, FFARCS, Lecturer in Anaesthesia, Sir Humphry Davy Department of Anaesthesia, University of Bristol, Bristol Royal Infirmary, Bristol.

0003–2409/86/040413 + 06 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

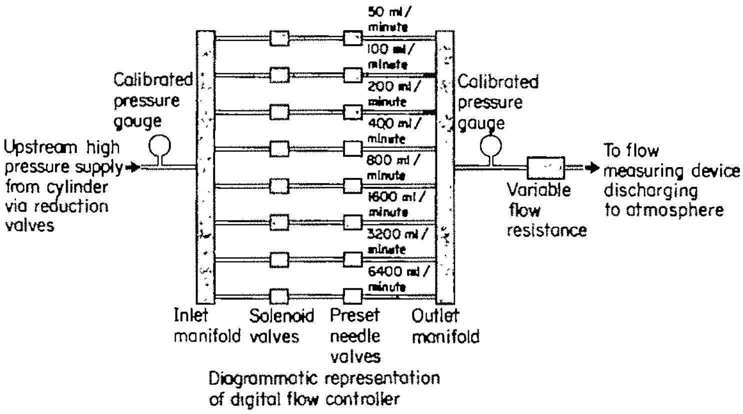

50 ml/minute
100 ml/minute
200 ml/minute
400 ml/minute
800 ml/minute
1600 ml/minute
3200 ml/minute
6400 ml/minute
Calibrated pressure gauge
Upstream high pressure supply from cylinder via reduction valves
Calibrated pressure gauge
Variable flow resistance
To flow measuring device discharging to atmosphere
Inlet manifold
Solenoid valves
Preset needle valves
Outlet manifold
Diagrammatic representation of digital flow controller

Fig. 1. Diagrammatic representation of prototype digital flow controller.

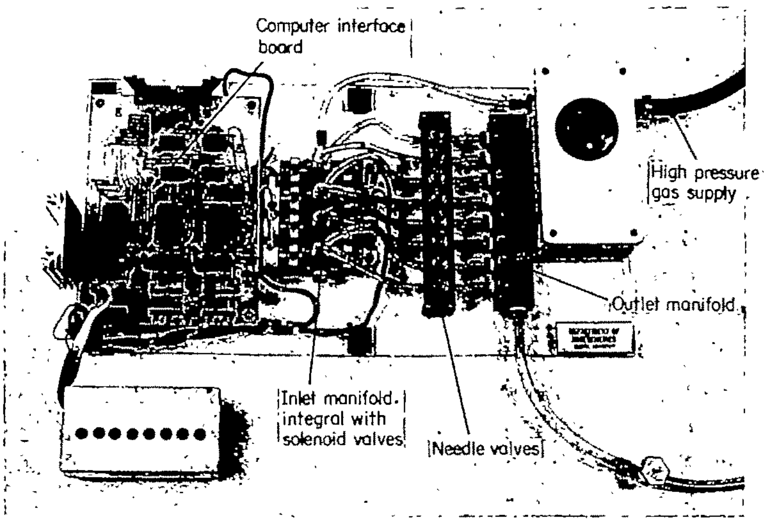


Fig. 2. Prototype digital flow controller.

on a microcomputer. This contains a program which rounds the set flow up or down to the nearest multiple of 50 ml/minute (there is a maximum theoretical inaccuracy of 25 ml/minute) and which controls the solenoid valves via an interface.

The technique of adding predetermined flows in a digital manner has been described previously for liquids by Langill *et al.*[3] (which is technically much easier), and for anaesthetic gases by Cooper *et al.*[4] Although they mention the use of sonic flows, the latter do not give any constructional details of the device they used.

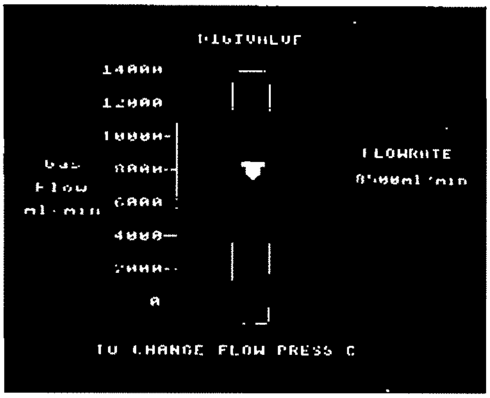
Design details

Several methods of presetting the flow in channel were examined, including narrow tubes, fixed nozzles, fixed orifices, sintered flow restrictors and needle valves. Apart needle valves, all the other methods are adjustable. They also depend upon very acc technically difficult and expensive mach processes. A literature search and enquiri several national laboratories revealed tha design of needle valves is largely empirical. the theory, if it ever existed, is lost in the mi time. Consequently, the flow characteristics of needle valves were examined in some detail and the results are to be published separately (unpublished observations[5]). In summary, it was found that at normal anaesthetic gas supply pressures, needle valves act effectively as variable annular nozzles, which possess critical flow properties. The importance of critical flow (sonic velocity in the nozzle throat) is that for a given upstream pressure and temperature, the mass flow rate of gas through the needle valve is unaffected by the variations in downstream pressure[6] which will be experienced in anaesthetic practice. This principle is used by engineers to meter accurately the flow of natural gas and the output from compressors.[7] The needle valve is thus a device with near ideal flow characteristics which may first be adjusted to give a desired flow and then locked into position. The ones used in our prototype were Clippard type MNV-2, capable of supplying up to 40 litres/minute of dry air, measured at ATP from an upstream pressure of 414 kPa gauge.

Two bubble flowmeters with volumes of 100 ml and 1550 ml were employed to calibrate the needle valves which had preset flows of 50, 100, 200, 400 and 800 ml/minute. These devices use a method originated by Barr,[8] in which the gas flow is passed through a vertical glass tube of known volume and the time taken for a soap film to pass between two fixed points is measured. Accuracy to better than 0.5 percent has been claimed[7] for this technique. Reference flows were provided for the valves passing the three largest flows (1600, 3200 and 6400 ml/minute by a Fisher Controls precision Rotameter (series 2100) calibrated to their accuracy grade A1 (0.5 percent indicated flow + 0.1 percent full scale reading). All the valves were calibrated with an upstream pressure and temperature of 414 kPa gauge and 20°C respectively and the outflow was corrected to a temperature of 20°C and a pressure of one atmosphere.

In any application in which a microcomputer is being used to control an electronic device, it is convenient to keep the power consumption of the unit to a minimum. Consequently, the solenoid valves chosen (Clippard model EV-2M) required only 0.68 watts to hold them open. These solenoid valves do not work in the normal manner; there is no moving core. The magnetic field generated attracts a spiral shaped metal diaphragm, the centre of which occludes an orifice. The valves have a low working temperature and are made from components compatible with 100% oxygen.

A BBC 'B' microcomputer was chosen to control the system, both because of the ease with which it can be used to drive electronic circuits and because of its graphics capabilities. The facilities of the BBC microcomputer and its use within the hospital environment have been discussed by Cowell.[9] When a flow is requested by the operator, the program converts it into an eight bit binary word, each bit (which can have the value 0 or 1) representing a solenoid valve being on or off. The information in the binary word leaves the computer by the 1MHz bus port and enters an interface circuit (an adaptation of a published design[10]), which converts the instruction into the appropriate voltages to power the solenoid valves. The valves are then automatically electronically latched until a new flow is programmed. The control program is written in Basic and the selected flow is displayed on the screen as the familiar Rotameter with a moving bobbin (Fig. 3).



TO CHANGE FLOW PRESS C

Fig. 3. BBC 'B' Microcomputer screen display to demonstrate gas flow rate.

System performance

The system may be tested in four ways to check that the principle of addition of the individually precalibrated flows works, to ensure the long term stability of the needle valve settings, to assess the errors produced by upstream variations in pipeline pressures, and to measure any changes in delivered flow as the downstream pressure is increased.

Using oxygen, the principle of addition of the eight channels was tested over the range 0–9000 ml/minute. The programmed oxygen flow was increased in steps of 50 ml/minute and the delivered flow (corrected to a temperature of 20°C and a pressure of one atmosphere) was measured by bubble flowmeter over the range 0–1000 ml/minute and by precision Rotameter from 1000–9000 ml/minute. To allow for permissible variation in medical pressures,[11,12] readings were made with supply pressures of 393, 414 and 434 kPa gauge. (These pressures were set by using a Bourdon gauge which had been calibrated against a Budenberg deadweight pressure gauge tester, Type 240). The results are shown in Figs 4 and 5.

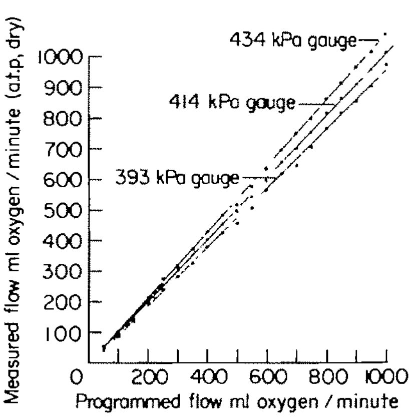


Fig. 4. A comparison of programmed and measured flows over the range 50–1000 ml/minute. The supply pressures are shown with x(ml/minute) as the programmed flow and y(ml/minute) as the measured flow. At a supply pressure of 393 kPa gauge, $y = 0.88 + 0.947x$, ($r = 0.998, n = 20$), at 414 kPa gauge, $y = 2.11 + 1.007x$, ($r = 0.999$, $n = 20$), and at 434 kPa gauge, $y = -2.48 + 1.072x$, ($r = 0.999$, $n = 20$).

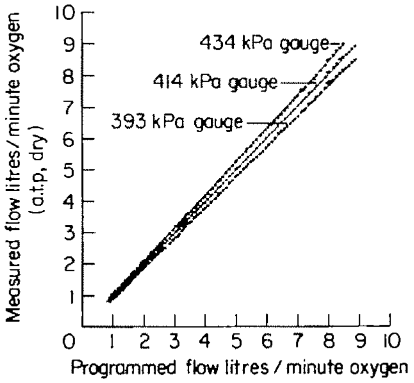


Fig. 5. A comparison of programmed and measured flows over the range 1–10 litres/minute. The supply pressures are shown with x(ml/minute) as the programmed flow and y(ml/minute) as the measured flow, at a supply pressure of 393 kPa gauge, $y = 49.0 + 0.96x$, ($r = 0.999$, $n = 101$), at 414 kPa gauge, $y = 22.0 + 1.0x$, ($r = 0.999$, $n = 101$), and at 434 kPa gauge, $y = -32 + 1.05x$, ($r = 0.999$, n 97).

To test the long term stability of the locked needle valves, requested flow rates of 1550 ml/minute, 3200 ml/minute and 8000 ml/minute were measured on 25 occasions at random intervals over a period of 3 months. These flows were chosen so that all the needle valves were used The coefficients of variation for the three flows were 0.8, 0.5 and 0.3% respectively.

To test the response of the digital valve to increasing downstream (or back) pressure (Fig. 1), the flow from the outlet manifold was passed through a variable resistance flow restrictor, which then discharged to atmosphere (Fig. 1) via the Rotameter or bubble flowmeter. In this way, with the supply pressure held constant, the back pressure on the needle valves could be gradually increased from atmospheric pressure (when the flow was maximum) to the supply pressure (when the flow was zero). At each level of increasing back pressure, the flow discharging from the variable restrictor (Fig. 1) was measured by the bubble flowmeter or precision Rotameter. The practical details of doing this are described elsewhere.[5]

The effects of increasing the back pressure on flows set initially at 1000 ml/minutes, 5000 ml/minute and 10 000 ml/minute, are shown in Fig. 6. The ratio of absolute downstream pressure to absolute upstream pressure on the abscissa was chosen to ensure similarity with our references on critical flow nozzles[6] and needle valves.[5]

Discussion

This paper has described the successful prototype development of a direct digital technique of controlling an anaesthetic gas flow which is simple to construct, has easy to use software, and a screen display representing the familiar Rotameter.

From Figs 4 and 5, it can be seen that its accuracy at the pipeline supply pressure of 414 kPa gauge (the typical set pressure in hospital systems[12]) is very high over the wide range of flows tested. This accuracy was maintained over the 3-month period of bench testing. It is, in fact, so accurate and stable that the calibrated

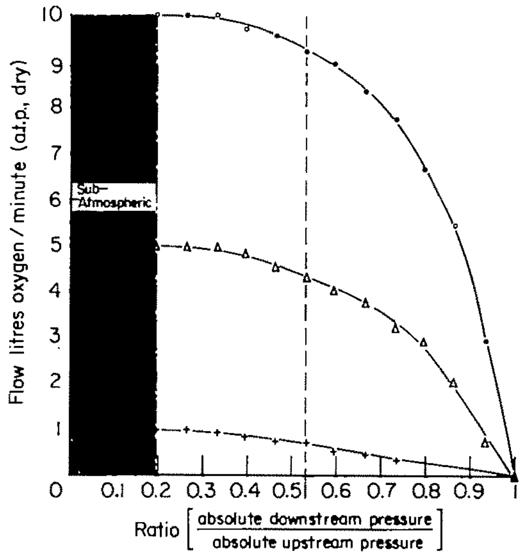


Fig. 6. The effect of increasing the back pressure on the flow through the prototype digital valve at three different settings. Supply pressure = 414 kPa gauge, atmospheric pressure = 103 kPa.

fixed nozzle with known upstream conditions may prove a challenge for existing standard flow measurement devices.

Figures 4 and 5 demonstrate the effect of the maximum permitted fluctuations in upstream pressure which occur in practice.[11] In piped medical gas systems, these changes are principally related to demand. Compensation for these variations could be achieved by monitoring the supply pressure with a transducer and using this signal as a correcting factor in the software. It should, however, be noted that the errors secondary to pipeline pressure changes described for this device are inherent in any flow which is fixed by a needle valve. A minute volume divider set from the usual Rotameter block in subject to exactly the same problem. This is discussed in more detail elsewhere.[5] In summary, a preset flow of 8000 ml/minute would deviate by a maximum of ± 368 ml/minute under the most extreme conditions permitted.

The accuracy obtained with the eight bit controller described is more than adequate for most clinical purposes and it may be that a six bit device would be sufficient. This would offer a least significant flow of 200 ml/minute and a maximum theoretical inaccuracy of 100 ml/minute, whilst retaining the same maximum flow of 12750 ml/minute.

It can be seen from Fig. 6 that the digital valve does not behave as a simple flow resistor. If it did, flow would fall (though not necessarily linearly) immediately the downstream/upstream pressure ratio increased from zero. The normal condition with the valve discharging to atmospheric pressure occurs at an absolute downstream/absolute upstream pressure ratio of 0.2. There is, however, no appreciable decrease in the discharged flow until this ratio increases to over 0.27, i.e., when the downstream pressure is 37 kPa gauge. This implies that if the digital valve were subjected to back pressure from an anaesthetic system or minute volume divider, it would have a negligible effect on the mass flow of gas delivered. The dotted line shown in Fig. 6 at a pressure ratio of 0.53 is the theoretical critical pressure ratio with oxygen for a perfect nozzle.[6] If the valves used in this construction were behaving as perfect isentropic nozzles, the performance curves would be flat up to this point. Further work[5] has shown that there is a considerable variation in needle valve performance depending on design; some, with physically larger internal dimensions, approach the ideal nozzle much more closely than the ones shown here. These would be incorporated in any future construction.

Tests with nitrous oxide gave results of an identical pattern to those with oxygen and are not shown. For clinical use, there are several refinements necessary. Gases would have to be filtered to ensure that no particulate matter adversely affects the solenoids, needle valves or patient. Delivering two gases (e.g. nitrous oxide/oxygen) with these devices requires fail safe mechanisms to be designed, which will not permit the delivery of hypoxic mixtures and which will allow manual override in emergencies. The operating theatre is also a 'noisy' electrical environment and microcomputers require special precautions to minimise electrical interference.

Work is, however, proceeding on the development of a three-channel device which will deliver nitrous oxide–oxygen and oxygen–air mixtures for use on patients. Apart from offering accurate flows and gas mixtures which could be used in the next generation of anaesthetic machines (at a competitive price with existing equipment), the device should, because of its computer control, be easily incorporated into an automatic closed loop control system. It is proposed to regulate the end-tidal carbon dioxide concentration of patients on controlled ventilation by using their own end-tidal carbon dioxide concentration as the feedback signal to control the fresh gas flow into a Bain system.

Other ideas under consideration are the automatic control of gas supply to cardiac bypass oxygenators and the simulation of continuously varying flows by using the device as a pneumatic A to D converter.

Acknowledgments

The authors would like to thank Professor C. Prys-Roberts for encouragement and discussion of the project and the Medical Physics Department for the construction of the apparatus. The equipment for the digital valve was purchased with a grant from the Nuffield Foundation (Grant Number SCI/168/237) and some of the computing hardware was obtained from the Bristol and Weston Health Authority District Medical Research Committee Project Grant 427.

References

1. Norman J. The I.V. administration of drugs. *British Journal of Anaesthesia* 1983; **55:** 1049–52.
2. Jelliffe RW. Open-loop-feedback control of serum drug concentrations: pharmacoki approaches to drug therapy. *Medical Instrum tion* 1983; **17:** 267–73.
3. Langill AW, Friedland H, Limbacher DL. control valve accepts digital systems. *Co Engineering* 1969; **16:** 94–98.
4. Cooper JB, Newbower RS, Moore JW, Tr man ED. A new anesthesia delivery system. *A thesiology* 1978; **49:** 310–8.
5. Hutton P, Boaden RW. The performanc needle valves. *British Journal of Anaesthesia* Press).
6. Shapiro AH. *The dynamics and thermodynami compressible fluid flow, Vol. 1.* New York: Ronald Press Co. 1953 pp. 91.
7. Ower E, Pankhurst RC. *The measurement o flow.* Pergamon Press. 1966 pp. 196, 250.
8. Barr G. Two designs of flowmeter and a met of calibration. *Journal of Scientific Instrum* 1934; **11:** 321–4.
9. Cowell TK. The BBC model B microcomput clinical instrumentation. *Journal of Me Engineering and Technology* 1983; **2:** 79–82.
10. Beverley P. Interface box for the Beeb. *Acorn* 1983; May, 53–64.
11. Department of Health and Social Security. Pi medical gases, medical compressed air and med vacuum installations. *Hospital Technical Me randum* 1977, No. 22.
12. DHSS. Permit to work system for medical ga medical compressed air and medical vacuum stallations (Suppl. to *Hospital Technical Me randum* No. 22.)

Anaesthesia, 1986, Volume 41, pages 419–422

Forum

The use of antacids as a prophylaxis against Mendelson's syndrome in the United Kingdom. A survey

B. Sweeney, FFARCS, FFARCSI, Senior Registrar, I. Wright, MRCP, FFARCS, Registrar, Department of Anaesthesia, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE.

Summary

Maternal mortality from aspiration of gastric contents still remains unacceptably high, despite various recommended prophylactic measures. In order to establish which forms of antacid prophylaxis are currently being used, a questionnaire was sent to anaesthetists working in obstetric units in the United Kingdom. Despite its limitations, magnesium trisilicate remains the most popular antacid during labour and before Caesarean section.

Key words

Gastrointestinal tract; stomach, pH.
Anaesthesia; obstetric.

The importance of pulmonary aspiration of acid gastric contents during obstetric anaesthesia has been recognised for 40 years.[1] It is common practice to attempt to prevent regurgitation and aspiration of gastric contents by the use of cricoid pressure. In addition, pharmacological methods of reducing the volume and increasing the pH of gastric contents, emptying of the stomach and avoidance of reduction in lower oesophageal sphincter tone are recommended.[2-8] It is clear from the last Confidential Report from England and Wales[9] that these measures are either ineffective or inappropriate for use on a busy labour ward. This survey was designed to identify current practice in aspiration prophylaxis in the United Kingdom.

Method

A questionnaire (Fig. 1) was designed to identify the choice of prophylaxis in labouring women, for elective Caesarean section and emergency Caesarean section. The drugs included in the questionnaire were magnesium trisilicate, sodium citrate and the histamine antagonists cimetidine and ranitidine. For the Caesarean section groups, metoclopramide and atropine were both included. In all three groups, a section was included for any other medications used. If a particular drug was used in any subgroup, the respondent was asked to give details of the dose, the route of administration and the frequency of administration. For the operative groups the timing, rather than the frequency, was included. Finally, the respondent was asked to append any other relevant comments.

The questionnaire was sent out in March 1984 to a total of 317 Departments of Anaesthesia in hospitals where obstetrics is performed. These departments were identified using a standard mailing list of a large pharmaceutical company. Each questionnaire was accompanied by a stamped addressed envelope which was coded.

Results

A response rate of 291 from 317 departments (91.8%) was obtained. The results were considered under three headings: active labour, elective Caesarean section and emergency Caesarean section.

Active labour. The results are tabulated in Fig. 2. No prophylaxis was used in 18.5% of units, 53.5% used mist magnesium trisilicate (46.7% alone), 23% used sodium citrate (12% alone), 3.4% used cimetidine (0.7% alone) and 11.3% used ranitidine (5.5% alone).

A combination of antacid and H_2-receptor blockers

© 1986 The Association of Anaesthetists of Gt Britain and Ireland

1. Is chemo-prophylaxis against acid aspiration syndrome normally given to patients who are in active labour in your Department?

Please tick ☐ YES ☐ NO

2. Which of the following agents are normally used, how much, how frequently and by what route are they given (O, IM, IV)?

	Please tick	Route	Amount	Frequency
Magnesium trisilicate				
0.3 M sodium citrate				
Cimetidine				
Ranitidine				
Other (please specify)				

3. For patients undergoing ELECTIVE Caesarean section is chemo-prophylaxis against acid aspiration syndrome routinely carried out in your Department?

Please tick ☐ YES ☐ NO

4. Which of the following agents are normally used? how much is given, by what route (O, IM, IV) and what is the timing in relation to induction of anaesthesia?

	Please tick	Route	Amount	Timing
Atropine				
Metoclopramide				
Magnesium trisilicate				
0.3 M sodium citrate				
Cimetidine				
Ranitidine				
Other (please specify)				

5. For patients undergoing EMERGENCY Caesarean section is chemo-prophylaxis against acid aspiration syndrome normally carried out in your Department?

Please tick ☐ YES ☐ NO

6. Which of the following agents are normally used? how much is given, by what route (O, IM, IV) and what is the timing in relation to induction of anaesthesia?

	Please tick	Route	Amount	Timing
Atropine				
Metoclopramide				
Magnesium trisilicate				
0.3 M sodium citrate				
Cimetidine				
Ranitidine				
Other (please specify)				

Please add any additional comments on reverse side

Fig. 1. The questionnaire used in the survey.

was used by 6.8%; the commonest was sodium citrate and cimetidine, 2.4%. Mist magnesium trisilicate and sodium citrate were used together by 5.2%. Other agents were used in less than 5%. Sodium bicarbonate predominated, although other antacids were occasionally used. Cimetidine was used almost exclusively orally, although ranitidine was usually administered parenterally.

Elective Caesarean section. The results are shown in Fig. 3. Mist magnesium trisilicate was used by 57% (25.1% alone), 36.4% used sodium citrate (14.1% alone), 8.6% cimetidine (1.7% alone), and 21% rantitidine (5.2% alone). Atropine was used by 26.5% (2.1% alone) and metoclopramide was used by 8.9%, but always in combination with other agents. No prophylaxis was used in 1.4% of units.

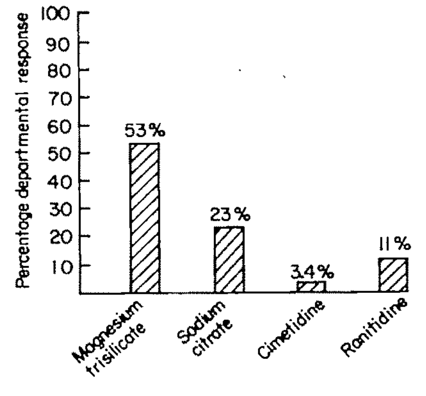


Fig. 2. Prophylaxis given to patients in active labour. No prophylaxis was used in 18.5% of departments.

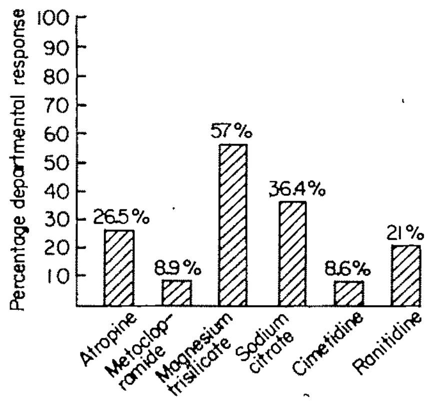


Fig. 3. Prophylaxis given to patients undergoing elective Caesarean section. No prophylaxis was used in 1.4% of departments.

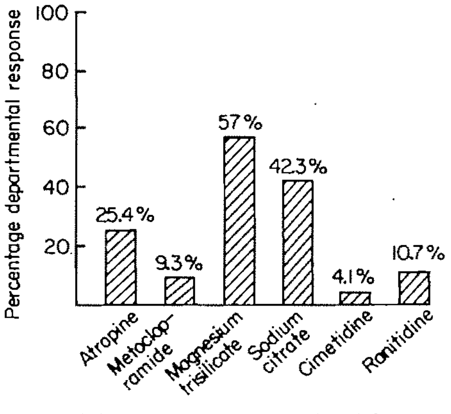


Fig. 4. Prophylaxis given to patients undergoing emergency Caesarean section. No prophylaxis was used in 0.7% of departments.

A combination of antacids and H-blockers was used by 9.3%; the commonest was sodium citrate and ranitidine and mist magnesium trisilicate and ranitidine, both in 2.7% of hospitals. Atropine was most commonly used in combination with mist magnesium trisilicate (11.7%), as was metoclopramide (1.7%). Other agents were used in less than 7% of cases, the commonest was sodium bicarbonate as an oral antacid, with atropine replaced by hyoscine as a premedicant. Cimetidine again was almost exclusively orally administered, while parenteral ranitidine was used in a similar proportion of cases as in active labour.

Emergency Caesarean section. The results are shown in Fig. 4. No prophylaxis was used in 0.7%, mist magnesium trisilicate by 57% (28.2% alone), sodium citrate by 42.3% (19.1% alone), cimetidine by 4.1% (0.3% alone), while 10.7% used ranitidine (0.3% alone). Atropine was used in 25.4% of units (2.1% alone) and 9.3% used metoclopramide (0.7% alone).

A combination of antacids and H_2-blockers was used in 12.4%; the commonest was sodium citrate and ranitidine 4.5%. Atropine was most commonly used in combination with mist magnesium trisilicate (12.4%) as was metoclopramide (3.1%). Other agents were used in less than 6%, sodium bicarbonate again being the most commonly used alternative while glycopyrronium sometimes replaced atropine. Intramuscular and intravenous cimetidine were used in 5% of cases. Ranitidine was used intramuscularly in 10% and intravenously in about 20% of cases.

Data relating to frequency and timing were not analysed due to the complexity of the various permutations used in clinical practice.

Discussion

The availability of a number of antacids, two histamine H_2-receptor antagonists and their use in three clinical situations allows a large number of possible combinations. Detailed consideration of every combination is of little value and the results were analysed to identify broad trends. These agree well with the results of a smaller survey published recently.[10]

It has been recommended that all women in active labour should be starved and receive antacid prophylaxis.[3] This advice was ignored in 20% of cases, surprising in view of the unpredictability of the need for operative intervention and the unreliability of preoperative single dose antacids alone in elevating gastric pH to safe levels. A small proportion (about 1%) of women undergoing Caesarean section also receive no prophylaxis. Even in the direst emergency, a dose of antacid helps to elevate the gastric pH, and a histamine H_2-receptor blocker elevates the pH to safe levels by the end of surgery, a time of almost as great a risk as induction.

In those departments which use some form of prophylaxis, the majority use magnesium trisilicate mixture. This is despite the inconvenience of 2-hourly administration (and thus the possibility of omission of a dose), the dangers of inhalation of a particulate antacid,[11] recent reservations as to the buffering capacity of the stored agent[12] and the increase in volume of gastric contents following its administration.

Of the histamine blockers, ranitidine is used more commonly than cimetidine, presumably reflecting the more convenient dose intervals. It is difficult to explain why it should be more popular for operative delivery, although cimetidine has been frequently implicated in drug interactions,[13] and has other agent-specific adverse effects.[14]

It has recently been postulated that a combination of histamine H_2-receptor blocker (especially ranitidine given 6-hourly) with a pre-operative nonparticulate antacid, is both the most effective and most convenient prophylactic regimen.[7] However, only 10% of respondents use such a regimen. It is interesting to speculate on the reasons for this. Although acid aspiration causes a disturbingly high proportion of preventable maternal deaths, it is still a rare event, to the extent that few anaesthetists have seen it. There is therefore less of a personal incentive to change established departmental policy in favour of one which may still be regarded as experimental. There may also be fears about the effect of H_2-blockers on the neonate, despite the work of McAuley *et al.*[6]

Atropine is used in about one quarter of operative deliveries. If used as a premedicant, it adversely affects lower oesophageal sphincter tone, although this may be avoided by using it as part of the induction sequence, in which case its effects are unlikely to be important. Perhaps the safest course is to use it only for its antimuscarinic properties in time of need, such as when repeated doses of suxamethonium have caused a bradycardia. Metoclopramide is used in about 10% of operative deliveries. In contrast to atropine, its use is to be recommended, although it is probably of more value as a premedication than used as part of the induction sequence.

There is wide variation in the policies for antacid prophylaxis. This probably indicates that no one regimen is clearly superior, although it may reflect a conservative approach to change. A consensus may be emerging, and suggestive evidence for this comes from the above mentioned survey of 22 departments. Five out of 22 currently who use antacids alone, and a further one use ranitidine only in elective Caesarean section, are considering a change in policy, presumably to include H_2-receptor antagonists. It would be interesting to repeat this survey in the future, to identify changes in practice stimulated by the large amount of recently published work.

Acknowledgments

We would like to thank Glaxo Laboratories Ltd. for their assistance with the survey.

References

1. Mendelson CL. The aspiration of stomach contents into the lungs during obstetric anesthesia. *American Journal of Obstetrics and Gynecology* 1946; **52:** 191–205.
2. Howard FA, Sharp DS. The effect of metoclopramide on gastric emptying during labour. *British Medical Journal* 1973; **1:** 446–8.
3. Crawford JS. The anaesthetist's contribution to maternal mortality. *British Journal of Anaesthesia* 1970; **42:** 70–3.
4. Frank M, Evans M, Flynn P, Aun C. Comparison of the prophylactic use of magnesium trisilicate mixture PBC., sodium citrate mixture or cimetidine in obstetrics. *British Journal of Anaesthesia* 1984; **56:** 355–62.
5. McCaughey W, Howe JP, Moore J, Dundee JW. Cimetidine in elective Caesarean section. Effect on gastric acidity. *Anaesthesia* 1981; **36:** 167–72.
6. McAuley DM, Moore J, Dundee JW, McCaughey W. Oral ranitidine in labour. *Anaesthesia* 1984; **39:** 433–8.
7. Gillett GB, Watson JD, Langford R. Ranitidine and single-dose antacid therapy as prophylaxis against acid aspiration syndrome in obstetric practice. *Anaesthesia* 1984; **39:** 638–44.
8. Skinner DB, Camp TF. Relation of oesophageal reflux to lower oesophageal sphincter pressures decreased by atropine. *Gastroenterology* 1968; **54:** 543–51.
9. Department of Health and Social Security. Tomkinson J, Turnbull A, Robson G, Dawson I, Cloake E, Adelstein AM, Ashley J, eds. *Report on confidential enquiries into maternal deaths in England and Wales. 1976–1978.* London: HMSO, 1982.
10. McDonald AG. The gastic acid problem. In: Atkinson RS, Adams AP (eds). *Recent advances in anaesthesia.* 1985; no. 15. London: Churchill Livingstone 107–32.
11. Bond VK, Stoelting RK, Gupta CD. Pulmonary aspiration syndrome after inhalation of gastric fluid containing antacids. *Anesthesiology* 1979; **51:** 452–3.
12. Crawford JS, Potter SR. Magnesium trisilicate mixture BP. Its physical characteristics and effectiveness as a prophylactic. *Anaesthesia* 1984; **39:** 535–9.
13. Klotz U, Reimann I. Delayed clearance of diazepam due to cimetidine. *New England Journal of Medicine* 1980; **302:** 1012–4.
14. Editorial. Cimetidine and ranitidine. *Lancet* 1982; **1:** 601–2.

Anaesthesia, 1986, Volume 41, pages 423–426

Intravenous feeding with medium chain triglycerides. Effect on blood gases and the complement system in critically ill patients

M. J. Ball, BSc, MB, BCh, MRCP, Clinical Lecturer, Nuffield Department of Clinical Biochemistry, J. W. Sear, BSc, PhD, FFARCS, DRCOG, Clinical Reader and Honorary Consultant in Anaesthetics, Nuffield Department of Anaesthetics, John Radcliffe Hospital, Headington, Oxford, Oxon OX3 9DU.

Summary

Critically ill patients are usually in a catabolic state and may require total parenteral nutrition; this often includes lipid emulsions. Any adverse effects of constituents on pulmonary function, white cell function or the haemocoagulation system could have disastrous consequences in such patients. We have investigated the effects of a new intravenous lipid preparation containing medium chain triglycerides, which, in severely ill malnourished patients are theoretically a preferable energy source to conventional drug chain triglycerides. In a pilot study 17 critically ill patients whose lungs were artificially ventilated were given this lipid emulsion; no adverse effects were observed. Arterial oxygen and carbon dioxide tensions, ratio of inspired oxygen fractional concentration to arterial oxygen tension, platelet and white cell counts all remained constant and the complement system was not activated.

Key words

Parenteral nutrition; triglycerides.
Complications.

The complement system is necessary for normal host defences. Activation has been reported to occur following severe burns and trauma,[1] thoracotomy[2] and cardiopulmonary bypass.[3] Some consider that activation of the complement cascade may be associated with the development of adult respiratory distress syndrome (ARDS), due partly to an effect on neutrophil aggregation.[4]

Total parenteral nutrition (TPN) is often administered to patients following major trauma or cardiothoracic surgery, but there is controversy over the effects of lipid emulsions on lung function and the safety of their use in the critically ill patient. Some reports have suggested that conventional long chain triglyceride emulsions (LCT) may be associated with the development of lung function abnormalities,[5-7] and that in the post-traumatic period, increased incorporation of lipid in the pulmonary vessels may lead to obstruction of the microcirculation and deterioration of pulmonary diffusion.[8] However, other studies have not found any adverse effects.[9,10] Thrombocytopaenia has also been reported in neonates receiving intralipid infusions.[11] In addition, LCT preparations require the amino acid derivative, carnitine, to facilitate their metabolism, and this may be depleted in the catabolic, malnourished patient.[12] Short and medium chain triglycerides (MCT) do not have this same requirement for carnitine. Short chain triglycerides have, however, been shown to cause rapid onset of pulmonary and haematological problems when given intravenously.[13] An intravenous lipid preparation containing MCT is now available and, if this can be used safely in all patients, it may prove to be a more effective metabolic fuel.

We have investigated the effects of this new lipid emulsion (Lipofundin MCT/LCT; B. Braun) containing 50 percent medium chain triglycerides, 50 percent long chain triglycerides in critically ill patients. Particular attention was directed to studying the effects on arterial blood gases, platelet counts, white cell counts and the complement system, with regard to cascade activation.

Methods

Seventeen patients, ASA 3 or 4, were studied 48–105 hours (mean: 80 hours) after admission to the intensive care unit (ICU). All the patients required intensive care and controlled positive pressure ventilation of their lungs following major trauma or abdominal surgery. The study was approved by the local Hospital Ethics Committee, and the patients were studied with the agreement of their relatives and/or the consultant in charge of the case. The patients (12 male, 5 female) were aged between 16 and 70 years, and their weights ranged from 50–75 kg. None of the patients was in renal or hepatic failure at the time of study. The study was performed at least 48 hours following the episode of

---

Correspondence should be addressed to Dr M. Ball, Nuffield Department of Clinical Biochemistry, Level 4, John Radcliffe Hospital, Headington, Oxford, OX3 9DU.

Table 1. Effect of medium chain triglyceride (MCT) infusion on arterial blood gases ($n = 17$)

	Pre-infusion	20 minutes post-infusion
Arterial $P\mathrm{o}_2$ (kPa)	10.6 (0.43)	10.7 (0.42)
Arterial $P\mathrm{co}_2$ (kPa)	4.92 (0.13)	4.91 (0.14)
Hydrogen ion concentration (nmol/l)	39.13 (0.90)	39.82 (0.91)

Mean (SEM); there was no significant difference between the variables (Wilcoxon matched pairs signed ranks test).

Table 2. Effect of medium chain triglyceride MCT infusion on complement levels and haematological parameters

	Pre-infusion ($n = 17$)	2 hours post-infusion ($n = 17$)	14 hours post-infusion ($n = 10$)
Platelet count ($\times 10^9$/litre)	246 (44)	243 (39.8)	253 (45)
White cell count ($\times 10^6$/litre)	13.9 (1.3)	14.4 (1.3)	14.2 (1.4)
% neutrophil leucocytes	82.2 (1.4)	82.6 (1.4)	—
Complement, C3 (mg/d litre)	124.3 (18)	130.3 (19.2)	128 (21)
Complement, C4 (mg/d litre)	17.4 (2.4)	19 (3.7)	18.2 (3.9)
C reactive protein (mg/d litre)	10.6 (5)	10.9 (4.2)	—

Mean (SEM); difference not significantly different by Wilcoxon test.

trauma or surgery, on patients whose only calorie source had been 5 percent dextrose infusion.

The lipid emulsion, Lipofundin 10 percent MCT/10 percent LCT (B. Braun), was infused via a central venous catheter at a rate of 3.5 mg/kg/minute over 3.5 hours. Glucose 5 percent was infused simultaneously via a peripheral cannula at a rate of 0.5 ml/minute. Continuous monitoring of pulse rate, blood pressure and electrocardiograph was performed.

Arterial blood samples were taken from an indwelling heparinised arterial line prior to the start of the lipid emulsion, after 3.5 hours at completion of the lipid infusion, and 20 minutes, 120 minutes and 14 hours after the end of the infusion. White cell counts and platelet counts were measured on EDTA specimens and complement components C3 and C4, and C-reactive protein (CRP) were measured in plasma from blood collected into lithium heparin tubes. Blood gases were measured on a pre-infusion sample and 20 minutes after the end of the infusion. Platelet counts, white cell counts, C3 and C4 were also measured at the end of a further infusion of 500 ml MCT/LCT given 24 hours later in three patients.

Methods of analysis. Blood gases were measured using an ABL 2 analyser (Radiometer, Copenhagen) calibrated against known standards. The white cells and platelet counts were performed using a Coulter S plus counter. The coefficients of variation for arterial carbon dioxide and oxygen tensions determinations on the ABL 2 analyser are 2.5 percent, and those on the Coulter S plus counter >2 percent for white cell counts and $<4\%$ for platelet counts. Blood films were also made and stained, and a visual differential white cell count performed. Complement components C3 and C4 and CRP were measured by nephelometry using the Beckman Immunochemistry systems analyser II (Beckman Instruments, Inc.).

Results

No significant change in any cardiovascular variable was observed during the lipid infusion. No patient showed clinical, biochemical or haematological sequelae which could be directly attributed to the lipid. The blood gas values for $P\mathrm{ao}_2$, $P\mathrm{aco}_2$ and hydrogen ion concentration are shown in Table 1. No significant changes were seen over the period of study and arterial oxygen tension/fractional inspired oxygen concentration ($P\mathrm{ao}_2/F\mathrm{io}_2$) ratio remained constant.

The results of the various haematological indices are shown in Table 2. During infusion of the lipid, the white cell count rose slightly. There was no evidence of any lipid-induced neutropaenia. The platelet count did not alter significantly and in no patient was a decrease of greater than 5 percent observed. The plasma levels of the complement components C3 and C4 remained stable. (Figs. 1 and 2). The three patients whose initial value of C3 were below the normal range (69–130 mg/d litre), showed no further decrease.

The levels of C-reactive protein before the fat infusion were markedly different in the various patients, but no acute rise occurred during the infusion. In the ten patients in whom data were available at 14 hours after the infusion, there were no subsequent changes in any of the above indices. In the three patients who received further infusions of MCT/LCT 24 hours later, no significant changes could be attributed to the second lipid infusion; complement levels did not fall in any of the patients.

Discussion

The choice of the non-amino acid component of parenteral nutrition is controversial. Many centres have used glucose alone or a mixture of glucose and lipid to

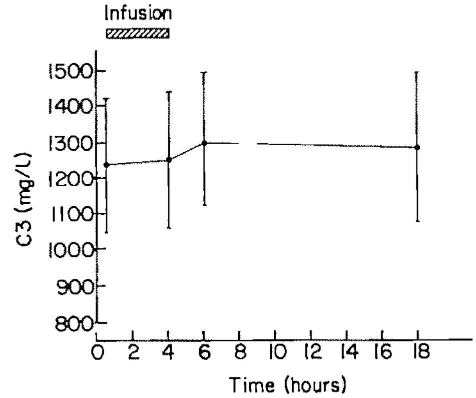


Fig. 1. Plasma concentration of C3 related to medium chain triglyceride/long chain triglyceride (MCT/LCT) infusion.

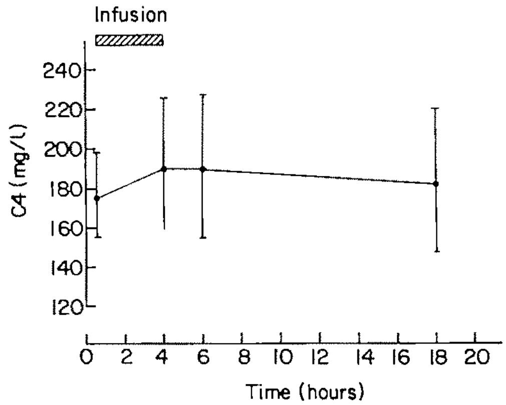


Fig. 2. Plasma concentration of C4 related to medium chain triglyceride/long chain triglyceride (MCT/LCT) infusion.

provide the main calorie source for ICU patients.[14] Recently it has been suggested that critically ill patients with sepsis are more dependent than non-septic patients on lipid fuels for oxidative metabolism.[15]

Lipid emulsions are metabolised to non-esterified fatty acids which are oxidised in cell mitochondria to provide energy in the form of adenosine triphosphate (ATP). However, long chain triglycerides require carnitine to enter the mitochondria. As carnitine may be depleted in critically ill patients,[12] there may be reduced capacity to metabolise these preparations. Medium chain triglycerides do not have the same requirement for carnitine, and thus may be a more rapidly utilisable substrate.

Conventional lipid emulsions are generally well tolerated, but there has been some concern about minor alterations in pulmonary function. Certain lipid preparations have been reported to reduce pulmonary diffusion capacity.[6] In one study in critically ill patients, 20 percent Intralipid (Kabi Vitrum Ltd.) caused no significant changes in the $Pa\text{O}_2/F\text{IO}_2$ ratio, mean pulmonary artery pressure, or pulmonary vascular resistance index when the pulmonary pathology was associated with intact alveolar capillary membranes (e.g. chronic obstructive lung disease or bacterial pneumonia). However, in patients with ARDS, where there is disruption of the alveolar capillary membrane, Intralipid caused decreased oxygenation, increased intrapulmonary shunting and a temporary increase in pulmonary artery pressure.[7] Venus *et al.* postulated that the absence of changes in pulmonary vascular resistance or pulmonary artery diastolic-pulmonary artery occlusion pressure gradient indicated that the changes may be due to capillary obstruction by fat and decreased oxygen diffusion.[7] The MCT/LCT preparation used in this study contains some 10 percent Lipofundin S. A study of the effects of Lipofundin S in patients with multiple injuries has not shown any changes in pulmonary artery pressure or alveolar–arterial oxygen difference when this lipid is infused.[10]

The effect of lipids on platelets is controversial. Reduction in platelet numbers was observed in some patients who were given the early lipid emulsions and there have been anecdotal reports of thrombocytopaenia in premature babies.[11] It is possible, however, that thrombocytopaenia in these babies may have been due to the underlying condition which necessitated the use of TPN. Nevertheless, minor effects on pulmonary function, neutrophil counts or platelets, or activation of the complement system, could have very serious consequences in critically ill patients at risk from ARDS, marrow suppression and sepsis.

Activation of the complement system has been linked to the development of ARDS in some circumstances. Complement activation can occur via two different pathways. The classical pathway is initiated by certain antigen–antibody complexes involving IgM and IgG, and plasma levels of both C4 and C3 fall when complement activation involves this pathway. Activation via the alternate pathway may be caused by bacterial endotoxins, thermally damaged cells, serum proteins and other factors and this causes a reduction in the circulating plasma level of C3. Complement activation results in the formation of potent active peptides, such as C3a and C5a, which are anaphylotoxins and stimulate the release of histamine from mast cells as well as causing an increase in vascular permeability. C5a is also able to bind to receptors on peripheral blood neutrophils and induce auto-aggregation and increased adherence.[16] It has been suggested that neutrophil aggregation due to the effects of activated complement components may contribute to the genesis of ARDS by the formation of micro-emboli. Hammerschmidt found a highly significant correlation between neutrophil aggregating activity and development of ARDS.[4]

Summary

Adult respiratory distress syndrome commonly develops following trauma, sepsis and pancreatitis. Patients with these conditions may be parenterally fed. For this reason, we chose to investigate traumatised and critically ill patients with sepsis, to study the effects of a new lipid emulsion containing MCT on complement activation. The results indicate that in the doses infused, this emulsion does not cause complement activation. Reduction in platelet and neutrophil numbers which could accentuate existing clinical problems did not occur within 14 hours after infusion. In addition, there was no significant reduction in Pao_2, or Pao_2/Fio_2 ratio. This study indicates that there are no obvious immediate adverse effects when MCT is used in critically ill patients. In view of its theoretical benefits, we are pursuing long term studies.

Acknowledgments

We would like to thank Dr A. Grant, Department of Clinical Biochemistry and the staff of the Intensive Care Unit, John Radcliffe Hospital, Oxford.

References

1. Gelfand JA, Donelan M, Burke JF. Preferential activation and depletion of the alternative complement pathway by burn injury. *Annals of Surgery* 1983; **198:** 58–62.
2. Haslam PL, Townsend PJ, Branthwaite MA. Complement activation during cardiopulmonary bypass. *Anaesthesia* 1980; **35:** 22–6.
3. Chenoweth DE, Cooper SW, Hugli TE, Steward RW, Blackstone EH, Kirklin JW. Complement activation during cardio-pulmonary bypass. Evidence for generation of C3a and C5a anaphylotoxins. *New England Journal of Medicine* 1981; **304:** 497–502.
4. Hammerschmidt DE, Weaver LJ, Hudson LD, Craddock PR, Jacob HS. Association of complement activation and elevated plasma-C5a with adult respiratory distress syndrome. Pathophysiological relevance and possible prognostic value. *Lancet* 1980; **2:** 947–9.
5. Levene MI, Wigglesworth JS, Desai R. Pulmonary fat accumulation after intralipid infusion in the preterm infant. *Lancet* 1980; **2:** 815–8.
6. Sundstrom G, Zauner CW, Arborelius M. Decrease in pulmonary diffusion capacity during lipid infusion in healthy men. *Journal of Applied Physiology* 1973; **34:** 816–20.
7. Venus B, Patel CB, Mathru M, Sandovel ED. Pulmonary effects of lipid infusion in patients with acute respiratory failure. *Critical Care Medicine* 1984; **12:** 293.
8. Eckart J. Diskussionsberkung In: Wretlind A. (ed.). Fettemulsions in der parenteralen Ernährung. Heidelberg, New York: Springer Verlag, 211–8.
9. Jarnberg PO, Lindholm M, Eklund J. Lipid infusion in critically ill patients. Acute effects on hemodynamics and pulmonary gas exchange. *Critical Care Medicine* 1981; **9:** 27–31.
10. Van Deyk K, Hempel V, Munch F, Kopp M, Graf H, Epple E. Influence of parenteral fat administration on the pulmonary vascular system in man. *Intensive Care Medicine* 1983; **9:** 73–7.
11. Lipson AH, Pritchard J, Thomas G. Thrombocytopenia after intralipid infusion in a neonate. *Lancet* 1975; **2:** 1462–3.
12. Nanni G, Pittiruti M, Castagneto M. Carnitine plasma levels during total parenteral nutrition (letter). *American Journal of Clinical Nutrition* 1983; **38:** 339–40.
13. Shafiroff BGP, Mulholland JH, Baron HC. Intravenous infusions into human subjects of fractionated coconut oil emulsions (19498). *Proceedings of the Society for Experimental Biology and Medicine* 1952; **79:** 721–3.
14. Abbott WC, Echenique MU, Bistrian BR, Williams S, Blackburn G. Nutritional care of the trauma patient. *Surgery, Gynecology and Obstetrics* 1983; **157:** 585–6.
15. Nanni G, Siegel JH, Coleman B, Fader P, Castiglione R. Increased lipid fuel dependence in the critically ill septic patient. *The Journal of Trauma* 1984; **24:** 14–30.
16. Craddock PR, Hammerschmidt D, White JG, Dalmasso AP, Jacob HS. Complement (C5a) induced granulocyte aggregation *in vitro*. *The Journal of Clinical Investigation* 1977; **60:** 260–4.

Anaesthesia, 1986, Volume 41, pages 427–446

Correspondence

Pharmacokinetics of fentanyl 428
C. Prys-Roberts, MD, DM, PhD, FFARCS
M. Wood, MD, FFARCS, C.S. Reilly, FFARCS and A.J.J. Wood, MRCP 429
Anaesthesia for extracorporeal lithotripsy 429
J.H. Pennant, FFARCS
M.A. Abbott, FFARCS, J.R. Samuel, FFARCS and D.R. Webb, FRACS 430
Safety features in oxygen analysers 430
P.G. Roe, BSc, MB, BS
Laryngeal cyst following fibreoptic intubation 430
B.L. Smith, FFARCS
Drowsiness after epidural opioids 431
I.S. Grant, FFARCSI, FRCP
The width of the posterior epidural space in obstetric patients 432
R.W.D. Nickalls, FFARCS and M.S. Kokri, FRCS, FFARCS
Coronary artery air embolism in the presence of nitrous oxide 433
K.M. Sherry, FFARCS and S. Sangwan, FFARCS
Pain with vecuronium 434
D.A. Cozanitis, MD
Delayed 'immediate' bupivacaine toxicity during axillary branchial plexus block 434
J.W. Mackenzie, MRCP, and J. Tytler, DRCOG, FFARCS
Topical adrenaline 435
N.R. Webster, PhD, FFARCS and W. Hinton, FFARCS
Acid aspiration 435
S. Liondas, MD
Difficult intubation due to unsuspected abnormality of the temporomandibular joint 436
H.K. Tey, FFARCSI
A hazard of the Penlon off-line vaporizer mounting system 437
R.H.K. Marsh, FFARCS and N.F. Thomas, MB, ChB
Survey on breathing system disconnexions 438
P.D. Neufeld, PhD, E.A. Walker and D.L. Johnson, PhD
Selectatec system: misplaced blood 439
J. Goddard, MRCP, FFARCS and T.R. Abbott, FFARCS
Two unilateral epidural blocks 439
G. Nunn, FFARCS and R.P.G. Mackinnon, MB, DRCOG
Premedication for children 440
A.J. Carter, FFARCS
Apparent postoperative recurarisation 440
N.M. Denny, FFARCS, D.W. Bethune, FFARCS, J.D. Kneeshaw, FFARCS, I. Hardy, FFARCS and R.D. Latimer, FFARCS
Oculocardiac reflex from the empty orbit 441
F.M. Khan, FFARCS, M.M. Ankutse, FFARCSI and R. Muhja, MS
Traumatic nasotracheal intubation 442
D.C. Harvey, FFARCS and P. Amoroso, MB, BS
A case for tonsillectomy 443
R. Cooper, MB, ChB
Intra-articular bupivacaine for pain relief in arthroscopic surgery 443
R.J. Eastley, FFARCS
Power failure in an intensive care unit 444
C.J.H. Johnson, MD, FFARCS
Unpredictable spread of heavy cinchocaine 444
C.A. Moore, DCH, FFARCS
The use of a biopsy brush wire as a bronchoscope guide 444
S.P. Gerrish, FFARCS and G. Weston, FFARCS
A problem with Murphy's eye 445
J.F. Harrison, FFARCS
Spinals 445
F.F. Casale, FFARCS
Rational metric doses of anticholinergic drugs 445
P. Radford, FFARCS
A further modification for direct arterial and central venous pressure monitoring 445
N.C. Huddy, FFARCS and A. Gaynor, FFARCS

All correspondence should be addressed to Dr J.N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

Letters must be typewritten on one side of the paper and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters contained in 'Notice to Contributors' to *Anaesthesia* printed at the back of each issue. The degrees and diplomas of each author must be given in a covering letter.

Correspondence presented in any other style or format may be the subject of considerable delay and may be returned to the author for revision.

Pharmacokinetics of fentanyl

The paper by Dr Reilly and his colleagues was interesting (*Anaesthesia*, 1985; **40**: 837–43) but I was surprised at their conclusions. Seven years ago I proposed the concept that low rate infusion of fentanyl was the only sensible way to maintain a constant pharmacodynamic effect (postoperative analgesia) at the cost of an acceptable degree of ventilatory depression. As a prelude to determining the appropriate infusion regimen I too searched for the necessary pharmacokinetic data. Unfortunately, at that time there were few *reliable* data available and we determined our own.[1,2] I was surprised then how consistent our results were, and how constrained were the plasma concentrations after a given dose of fentanyl. Subsequently, we applied our data to the prediction of an infusion regimen for postoperative pain relief[3] and found that we achieved the predicted plasma concentration and the pharmacodynamic side effect of ventilatory depression with remarkable consistency.

Why then do Dr Reilly and his colleagues find that fentanyl pharmacokinetics *appear* to be inconsistent and unpredictable, whereas I did not? For the simple reason that they tried to base their single dose and infusion regimens on 'population' pharmacokinetics derived from the literature. Let us examine their sources carefully to find why their results are so disparate.

There is no reason why data derived from conscious volunteers should be appropriate for predicting the disposition of a drug in anaesthetised patients. Indeed, Hug showed that this was precisely the case for fentanyl and other opioids.[4] Thus, the data from Bower and Hull,[5] and McClain and Hug[6] clearly show higher clearance, yet, paradoxically, longer elimination half-times than those found in anaesthetised patients. This is because the drug, being highly lipid soluble, is distributed in a rather larger total volume of distribuion (*c.* 4–5 litre/kg) compared with the values found during anaesthesia (1–3 litre/kg). Presumably, the anaesthetised patient subject to surgery is more vasoconstricted than his awake volunteer counterpart; thus, drugs are distributed in a smaller volume. The clearance of fentanyl during anaesthesia is markedly lower than in awake subjects[4] and may be further lowered by a number of factors which decrease liver blood flow such as hypocapnic hyperventilation.[2] Many of the earlier studies[7,8] quoted by Dr Reilly and colleagues were based on radioimmunoassay techniques whose specificity has been called into question.[4,9] Another[10] was based on a gas liquid chromatographic method whose accuracy is very suspect at the lower concentrations encountered at the later periods in the multi-exponential decay of drug concentration,[2] and which therefore influence the derived pharmacokinetic parameters. Note that in Bentley's paper, the coefficient of variation of the assay is only quoted at plasma concentrations of 250 and 1000 ng/ml, well above the range of values normally found during anaesthesia.

Dr Reilly and his colleagues do us a great disservice by suggesting that 'the pharmacokinetics of fentanyl are insufficiently consistent to be of assistance to the anaesthetist in choice of dosage regimen'. My experience, and that of my colleagues in Bonn,[11] has been quite the opposite. That it has been so was the result of using pharmacokinetics determined under the precise conditions relevant to those to be considered for the prediction. Studies on awake volunteers are only relevant to awake subjects of the same age, not under the influence of other drugs. In order to predict dose requirements for intravenous infusions of drugs during and after anaesthesia, one must rely only on data derived under the same conditions.

Sir Humphry Davy Department of Anaesthesia,
University of Bristol,
Bristol Royal Infirmary,
Bristol BS2 8HW

C. PRYS-ROBERTS

References

1. GILL KJ, CARTWRIGHT DP, SCOGGINS A, GRAY AJ, PRYS-ROBERTS C. Ventilatory depression related to plasma fentanyl concentrations during and after anaesthesia. *British Journal of Anaesthesia* 1980; **52**: 632P.
2. CARTWRIGHT P, PRYS-ROBERTS C, GILL K, DYE A, STAFFORD M, GRAY A. Ventilatory depression related to plasma fentanyl concentrations during and after anesthesia in humans. *Anesthesia and Analgesia* 1983; **62**: 966–74.
3. ANDREWS CJH, SINCLAIR M, PRYS-ROBERTS C, DYE A. Ventilatory effects during and after continuous infusion of fentanyl or alfentanil. *British Journal of Anaesthesia* 1983; **55**: Supplement 2; 211S–65.
4. HUG CC, Jr. Pharmacokinetics and dynamics of narcotic analgesics. In: Prys-Roberts C, Hug CC Jr, Eds. *Pharmacokinetics of anaesthesia.* Oxford: Blackwell, 1984: 187–234.
5. BOWER S, HULL CJ. Comparative pharmacokinetics of fentanyl and alfentanil. *British Journal of Anaesthesia* 1982; **54**: 871–7.
6. MCCLAIN DA, HUG CC. Intravenous fentanyl kinetics. *Clinical Pharmacology and Therapeutics* 1980; **28**: 106–14.
7. SCHLEIMER R, BENJAMINI E, EISELE J, HENDERSON G. Pharmacokinetics of fentanyl as determined by radioimmunoassay. *Clinical Pharmacology and Therapeutics* 1978; **23**: 188–94.
8. FUNG DL, EISELE JH. Fentanyl pharmacokinetics in awake volunteers. *Journal of Clinical Pharmacology* 1980; **20**: 652–8.
9. MATHER LE. Clinical pharmacokinetics of fentanyl and its newer derivatives. *Clinical Pharmacokinetics* 1983; **8**: 422–46.
10. BENTLEY JB, BOREL JD, NENAD RE, GILLESPIE TJ. Age and fentanyl pharmacokinetics. *Anesthesia and Analgesia* 1982; **61**: 968–71.
11. SCHÜTTLER H, SCHWILDEN H, STOECKEL H. Infusion strategies to investigate the pharmacokinetics and pharmacodynamics of hypnotic drugs: etomidate as an example. *European Journal of Anaesthesiology* 1985; **2**: 133–42.

A reply

We are grateful to Professor Prys-Roberts for his comments. However, he seems to have missed the point of our study. We did not use population data to predict concentrations during surgery. In fact, we used the pharmacokinetic data from a number of studies to simulate, by computer, the concentrations which each of the studies predicted would have been produced in the author's own populations with the dosage regimens chosen. In that situation we found that there was enormous variability in the predicted plasma fentanyl concentrations. The publication of data describing a drug's pharmacokinetic properties is presumably of value only if it allows readers to predict more accurately drug concentrations in their own patients. In our view, as demonstrated in our paper, the difference between the various published studies renders such prediction problematic.

We are pleased to hear that Professor Prys-Roberts found that his own data accurately predicted plasma fentanyl concentrations during infusion, but his paper,[1] which he cites as evidence to support this, did not allow us to share his confidence. We can find only one mean plasma fentanyl value quoted in the entire paper and that appears to have been drawn one hour after the fentanyl infusion was stopped. Thus, we can find no data to support his claim to have achieved the predicted plasma fentanyl concentrations. Data are presented in his paper neither of plasma fentanyl concentrations over the time period of the infusion, nor of how closely each individual's values matched the predicted value for that individual at the various time points.

The effects of anaesthesia on drug disposition were discussed in our paper and are well-known to us as we have recently shown the effects of a number of anaesthetics on drug metabolism and disposition.[2-5] However, as we stated in our paper, although within study differences in fentanyl kinetics between healthy controls and surgical patients have been described, these did not explain our findings. For example, the normal volunteer studies quoted yielded values that were amongst both the highest and the lowest in our simulations.

Thus, we remain convinced that there is considerable inconsistency in the plasma fentanyl concentrations which would be predicted from the various published studies describing fentanyl pharmacokinetics.

Department of Pharmacology,
School of Medicine,
Vanderbilt University
Nashville,
Tennessee 37232
USA

MARGARET WOOD
C.S. REILLY
A.J.J. WOOD

References

1. ANDREWS CJH, SINCLAIR M, PRYS-ROBERTS C, DYE A. Ventilatory effects during and after continuous infusion of fentanyl or alfentanil. *British Journal Anaesthesia* 1983; **55:** Supplement 2: 211S–6S.
2. WOOD M, WOOD AJJ. Contrasting effects of halothane, isoflurane, and enflurane on *in vivo* drug metabolism in the rat. *Anesthesia and Analgesia* 1984; **63:** 709–14.
3. REILLY CS, WOOD AJJ, KOSHAKJI RP, WOOD M. The effect of halothane on drug disposition: Contribution of changes in intrinsic drug metabolizing capacity and hepatic blood flow. *Anesthesiology* 1985; **63:** 70–6.
4. GORDON L, WOOD AJJ, WOOD M. Acute effects of halothane on drug distribution in the dog. *Anesthesia and Analgesia* 1985; **64:** 219.
5. REILLY CS, WOOD AJJ, KOSHAKJI R, WOOD M. The effect of fentanyl anesthesia on drug disposition. *Anesthesiology* 1985; **63:** A280.

Anaesthesia for extracorporeal lithotripsy

The interesting paper from Drs Abbott, Samuel and Webb (*Anaesthesia* 1985; **40:** 1065–72) describing anaesthesia for extracorporeal shock wave lithotripsy (ESWL) omits to mention a few points of anaesthetic importance.

Great care must be taken when the arms of anaesthetised patients are positioned on the hydraulic cradle, to prevent brachial plexus stretch injuries. This potential hazard can be prevented by using a regional technique, because then the awake patient can position himself comfortably in the frame.[1]

Respiratory excursion of the diaphragm moves the renal calculus away from the focal point of the ellipsoidal reflector, so that much of the shock wave energy is dissipated in other biological tissues; this undoubtedly contributes to postoperative morbidity. A proportion of shock waves miss their target, so a larger number of discharges are required to fragment the calculus, and this makes the procedure more expensive and prolonged. This problem can be minimised by asking the patient to take shallow breaths. In the case of patients under general anaesthesia, rapid respiratory rates and small tidal volumes enable the renal calculus to be kept in focus for most of the respiratory cycle. The logical solution is to use some form of high frequency positive pressure ventilation.

Finally, the incidence of postoperative colic may be reduced by a diuresis, which flushes blood clots and calculus fragments through the renal tract in all patients undergoing ESWL. However, this must be done cautiously in patients with cardiovascular disease.

Department of Anaesthetics,
King's College Hospital,
London, SE 58RX

J.H. PENNANT

Reference

1. DUVALL JO, GRIFFITH DP. Epidural anesthesia for extracorporeal shock wave lithotripsy. *Anesthesia and Analgesia* 1985; **64**: 544–6.

A reply

We thank Dr Pennant for his helpful comments. We agree that care must be taken in positioning patients, no matter what the procedure. It should be emphasised that in ESWL, the arms are positioned partially abducted and flexed. Patients who have surgical procedures with their arms abducted on an armboard to or beyond the coronal plane are significantly more at risk. No injuries of this type have been reported and we consider that this must not be regarded as a major factor in the choice of anaesthetic technique.

The validity of his recommendation for the use of high frequency positive pressure ventilation is borne out by its adoption subsequent to the series of patients described in our paper, these being the first treated in this country.

We quite agree that an induced diuresis encourages clot and fragment removal. Diuretics were routinely administered at the end of the procedure. However, if this manoeuvre is not accompanied by a waterload, the initial increase in urine flow will be followed by a period of oliguria. It is therefore more important to maintain an increased urine output throughout the first 24, and preferably the first 48, hours by a high oral intake plus intravenous supplements if clinical conditions indicate.

Research Department of Anaesthetics, M.A. ABBOTT
Royal College of Surgeons of England, J.R. SAMUEL
35, Lincoln's Inn Fields, D.R. WEBB
London, WC2A 3PN

Safety features in oxygen analysers

A recent study of current fuel cell oxygen analysers included the Oxydig (Drager Medical). Drager have recently brought out a new version of this, which has a number of modifications, of which one is worthy of comment. The new analyser is programmed to enter an 'Inop' mode at oxygen concentrations of <5% which correspond to a fixed minimum current generated by the sensor cell. No further oxygen readings are displayed until the monitor has been switched off and on and recalibrated. There are two reasons for this. First, low current from the sensor may be due to sensor disconnexion or malfunction. Second, it is claimed that inaccurate readings may result from a sensor that has been exposed to zero oxygen. Our experiments have, however, shown that the original version, which read down to zero, maintained an acceptable accuracy despite an hypoxic insult.

There are situations in anaesthesia where the oxygen concentration may fall to zero and where the presence of an oxygen analyser is important, not only to indicate this but also to ascertain that corrective measures have succeeded in returning the inspired oxygen concentration to acceptable levels. This may not be the case in event of a pipeline crossover, and the new version would not indicate this. It would be preferable to maintain the display of the oxygen concentration and to display a calibration request at the same time.

Magill Department of Anaesthetics, P.G. ROE
Westminster Hospital,
London, SW 1P 2A

Laryngeal cyst following fibreoptic intubation

A 16-year-old male with juvenile chronic arthritis (formerly Still's disease) since the age of 5 years was scheduled for bilateral total hip replacement.

On pre-operative examination he showed the stigmata of early onset of juvenile chronic arthritis, with diminished stature, polyarthritis, shortened mandible, stiff neck, relatively large tongue and prominent top front teeth. He was obese from steroid therapy and inactivity.

The anaesthetic method was as described earlier,[1,2] with trimeprazine as premedication, gaseous induction, intravenous ketamine, topical anaesthetic to nose and larynx and then guided nasotracheal intubation with a fibreoptic rhinoscope. Spontaneous ventilation was maintained throughout and the surgery proceeded under nitrous oxide and halothane anaesthesia with increments of propranolol and fentanyl. A clear view of the larynx was obtained at intubation, but a certain amount of firm manipulation was required to pass the tracheal tube over the rhinoscope and into the trachea. Extubation after full recovery postoperatively was uneventful.

Three months later the patient was rescheduled for the second hip procedure and the same anaesthetic sequence was embarked upon. On this occasion, a 1.5 cm mucous cyst was observed above the larynx, which arose from the posterior arytenoid area. The fibrescope was manoeuvred with some difficulty past this obstruction. A tracheal tube was manipulated into the trachea over the rhinoscope, but on withdrawal of the latter, the tube kinked and obstructed. It was therefore withdrawn and the technique abandoned in favour of spinal anaesthesia and sedation with Entonox. This proved effective and surgery was completed without further problems.

Postoperatively, the parent gave a history of two months dysphagia and weight loss following the original hip procedure. Subsequently, using the same rhinoscope, under ketamine and local anaesthetic, the mucous cyst was incised and deroofed, and a clear glairy fluid was released. Three weeks later there was no sign of the cyst and the child was eating well and was uncomplaining.

Accounts of crico-arytenoid arthritis in juvenile chronic arthritis are well documented,[3,4] but the formation of a laryngeal mucous cyst after intubation is not. It is reported since it is a potentially hazardous sequel of guided intubation with a fibre optic device with the inevitable minor trauma that accompanies this procedure.

Wexham Park Hospital,
Slough, Berkshire

B.L. SMITH

References

1. D'ARCY EJ, FELL RH, ANSELL BM, ARDEN GP. Ketamine and juvenile chronic polyarthritis (Still's disease). Anaesthetic problems in Still's disease and allied disorders. *Anaesthesia* 1976; **31:** 624–32.
2. SMITH BL. Anaesthesia and Still's disease. *Anaesthesia* 1985; **40:** 209.
3. SCHLESINGER BE, FORSYTH CC, WHITE RHR *et al. Observations on the clinical course and treatment of one hundred cases of Still's disease. Archives of Disease in Childhood* 1961; **36:** 65–76.
4. JACOBS JC, HUI RM. Cricoarytenoid arthritis and airway obstruction in juvenile rheumatoid arthritis. *Pediatrics* 1977; **59:** 292–4.

Drowsiness after epidural opioids

Frequency of respiratory depression as a complication of epidural opioid administration depends, amongst other factors, on the lipid solubility of the agent used, the dose administered and the site of injection.[1] Highly lipid soluble agents such as diamorphine or fentanyl are rarely associated with respiratory depression, on account of their rapid cerebrospinal fluid (CSF) clearance in contrast to the more hydrophilic morphine.[2,3]

Nevertheless, caution should be exercised in the use of epidural opioid analgesia even with the more lipophilic agents, especially when the thoracic site is used for injection, since CSF circulation time to the brain stem is reduced. The following is a report of a case of repeated respiratory depression and extreme drowsiness associated with thoracic epidural diamorphine analgesia after thoracotomy.

A previously fit 64-year-old man scheduled for total gastrectomy through a left thoraco-abdominal incision was premedicated with temazepam 20 mg orally. Anaesthesia was induced with thiopentone, double-lumen tracheal intubation was facilitated by suxamethonium, muscle relaxation continued with alcuronium, and anaesthesia maintained with 66% nitrous oxide and 0.5% halothane in oxygen. Monitoring included central venous pressure measured via a right internal jugular line and radial arterial pressure. A thoracic epidural catheter was placed at mid-thoracic level and 0.5% bupivacaine 7 ml injected after induction of anaesthesia. Surgery lasted 5 hours; 15 minutes before the completion of surgery, diamorphine 2.5 mg in 5 ml bupivacaine 0.25% and 1:200000 adrenaline was injected through the epidural catheter. Neuromuscular blockade was reversed with intravenous neostigmine 2.5 mg and atropine 1.2 mg and, following satisfactory restoration of spontaneous ventilation, the trachea was extubated and the patient transferred to the intensive care unit.

One hour after the epidural diamorphine injection, the patient became very drowsy and his ventilation shallow, although the respiratory rate remained at 14 breaths/minute. Arterial blood gas estimation revealed a $Pa\text{CO}_2$ of 9.5 kPa. The patient became fully awake, with a respiratory rate of 30/minute, after intravenous naloxone 0.2 mg; he had an arterial $Pa\text{CO}_2$ of 6.2 kPa and was still pain free.

Excellent analgesia was maintained for 8 hours, when a second injection of diamorphine 2.5 mg in 5 ml 0.9% saline with 1:200000 adrenaline was given. No drowsiness or obvious respiratory respiratory depression occurred on this occasion, but an arterial $Pa\text{CO}_2$ estimation 1 hour after injection was 7.3 kPa. A third injection of epidural diamorphine 2.5 mg in 5 ml 0.9% saline with 1:200000 adrenaline 11 hours later was followed again by extreme drowsiness 4 hours later, with an arterial $Pa\text{CO}_2$ of 8.4 kPa, although the respiratory rate was 20 breaths/minute. Intravenous naloxone 0.2 mg again awoke the patient fully without pain and restored the arterial $Pa\text{CO}_2$ to 6.2 kPa.

The patient had an otherwise excellent, pain and complication-free, postoperative period. Later, intramuscular injections of morphine, 10 mg, caused no undue sedation or respiratory depression.

This case illustrates that respiratory depression may occur even after a small dose, 2.5 mg, of a lipid soluble opioid, diamorphine. Addition of 1:200000 adrenaline to decrease systemic uptake may have resulted in greater CSF concentration and brain stem uptake of diamorphine.[4] Alternatively, in view of the early respiratory depression in the first instance, it may be that rostral spread occurred through the internal vertebral venous system, possibly as a result of raised intrathoracic pressure due to artificial ventilation.[1]

The extreme sedation seen here is not generally remarked upon in the literature, but has been reported in some clinical studies.[5] It is noteworthy that it was dramatically improved by naloxone. This case also emphasises that the respiratory rate is an unreliable guide to respiratory depression; in patients at high risk of this complication, notably those in whom thoracic epidural opioid analgesia has been administered, arterial blood gases should be checked.

In conclusion, epidural opioid analgesia, even using a lipid soluble agent such as diamorphine, may result in respiratory depression. Its likelihood may be influenced by the use of the thoracic route, the dose of agent used, addition of adrenaline and by concurrent controlled ventilation at the time of injection. Careful respiratory monitoring is essential.

Department of Anaesthesia,
Ninewells Hospital,
Dundee, DD1 9SY

I.S. Grant

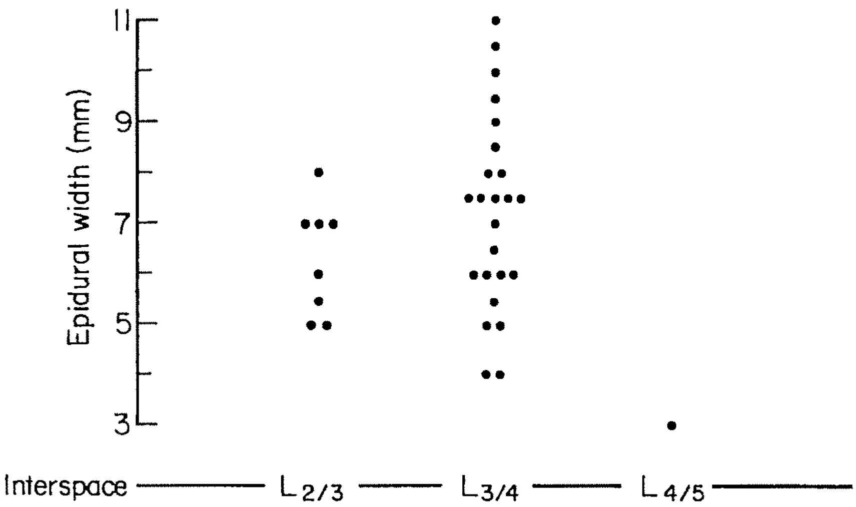
References

1. Cousins MJ, Mather LE. Intrathecal and epidural administration of opioids. *Anesthesiology* 1984; **61:** 276–310.
2. Moore R, Bullingham R, McQuay H, Allen M, Baldum D, Cole A. Spinal fluid kinetics of morphine and heroin. *Clinical Pharmacology and Therapeutics* 1984; **35:** 40–5.
3. Lam AM, Knill RL, Thompson WR, Clement JL, Varkey GP, Spoerel WE. Epidural fentanyl does not cause delayed respiratory depression. *Canadian Anaesthetists' Society Journal* 1983; **30:** 578–9.
4. Bromage PR, Camporesi EM, Durant PA, Nielsen CH. Influence of epinephrine as an adjuvant to epidural morphine. *Anesthesiology* 1983; **5:** 257–62.
5. Bromage PR, Camporesi E, Chestnut D. Epidural narcotics for postoperative analgesia. *Anesthesia and Analgesia* 1980; **59:** 473–80.

The width of the posterior epidural space in obstetric patients

The interest currently being shown in the combined spinal epidural technique prompts us to publish some data we have on the width of the epidural space in obstetric patients. We have been using a recently described modification of this combined technique[1] to estimate the width of the posterior epidural space in the midline, in 33 patients for Caesarean section.

All patients were in the left lateral position, and great care was taken to advance the Tuohy needle (16-G) slowly enough to avoid pushing it further than necessary into the epidural space, which was detected by the loss of air resistance. A spinal needle (26-G; 15-cm) was then advanced through the Tuohy needle with similar caution, and clamped with a pair of small lightweight artery clips as soon as the dura was felt to have been pierced. The spinal needle, with artery clip still attached, was re-inserted after the procedure into the Tuohy needle, and the length of spinal needle protruding from the end was measured to the nearest half millimetre. This length was taken as an index of the width of



Interspace	L2/3	L3/4	L4/5
n	8	24	1
Mean ±SD	6.3±1.1	7.2±1.9	3
Range	5–8	4–11	

epidural space, on the assumption that both the Tuohy and the spinal needle had entered their respective epidural and dural spaces to approximately the same depth.

The results for each lumbar interspace are shown in the figure. Neither patient height (measured at the booking clinic) nor lumbar interspace number showed any significant correlation with epidural width. The results were therefore pooled ($n = 33$): the mean (SD) epidural width was 6.8 (1.9) mm and the mean (SD) height was 1.57 (0.06) m.

Published data regarding the width of the adult posterior lumbar epidural space are both sparse and indirect and there are none for obstetric patients. Bromage[2] indicates that this space is greatest in the midline '... in the second lumbar interspace, where the distance is about 5–6 mm in adult males. However, he gives no supporting reference for this statement. Bonica[3] gives the range as '... 4–6 mm in the lumbar region'. In a dissection study, Cheng[4] gives a value of 6 mm for '... the average person'. Resin cast data from cadavers suggest ranges of 2–9 mm[5], and 1–9 mm[6]. However, in the latter study, widths greater than 3 mm were associated with posterior compression of the dural sac. In a recent detailed dissection study of the lumbar epidural space[7] the width of the posterior epidural space was not measured. Myelographic data do exist[8] for the posteriolateral and anterior lumbar epidural spaces, but not for the space in the midline posteriorly. Meaningful comparison is therefore very difficult. Even so, our values, which we believe are the first published measurements in obstetric patients, do not differ significantly from those already published.

Department of Anaesthetics,
The Royal Victoria Infirmary,
Newcastle-upon-Tyne,
NE1 4LP

R.W.D. Nickalls
M.S. Kokri

References

1. Nickalls RWD, Dennison B. A modification of the combined spinal and epidural technique. *Anaesthesia* 1984; **39:** 935–6.
2. Bromage PR. *Epidural analgesia.* London: Saunders, 1978: 13–4.
3. Bonica JJ. *Principles and practice of obstetric analgesia and anaesthesia.* Oxford: Blackwell Scientific Publications, 1967: p. 622.
4. Cheng PA. The anatomical and clinical aspects of epidural anesthesia. Part I. *Anesthesia and Analgesia* 1963; **42:** 398–406.
5. Husemeyer RP, White DC. Topography of the lumbar epidural space. A study in cadavers using injected polyester resin. *Anaesthesia* 1980; **35:** 7–11.
6. Harrison GR, Parkin IG, Shah JL. Resin injection studies of the lumbar extradural space. *British Journal of Anaesthesia* 1985; **57:** 333–6.
7. Parkin IG, Harrison GR. The topographical anatomy of the lumbar epidural space. *Journal of Anatomy* 1985; **141:** 211–7.
8. Lewit K, Sereghy T. Lumbar peridurography with special regard to the anatomy of the lumbar peridural space. *Neuroradiology* 1975; **8:** 233–40.

Coronary artery air embolism in the presence of nitrous oxide

We wish to report a complication which has arisen in two patients at this hospital during surgery for coronary artery vein grafts in the past 4 months. Both patients were admitted for elective surgery and angiography indicated good left ventricular function. The anaesthesia was a benzodiazepine, opiate, relaxant technique and the lungs were ventilated with nitrous oxide 50% in oxygen prior to cardiopulmonary bypass. The lungs were ventilated with 100% oxygen and the perfusion was withdrawn after completion of aortocoronary grafting. Neither patient required inotropic support. The cardiovascular status of both patients remained stable for 20 minutes and arterial blood analysis confirmed good oxygenation, acid base balance and serum potassium. Nitrous oxide, 50%, was introduced at this time to the inspired mixture and, within a few minutes, both patients developed ST-segment depression accompanied by a decrease in systolic blood pressure to between 60 and 70 mmHg. In the first patient, a nitroglycerine infusion failed to modify the clinical condition, but improvement was quickly apparent when nitrous oxide was withdrawn. In the second patient, nitrous oxide was stopped immediately, the ST segments returned to the baseline and systolic blood pressure rose to 100 mmHg. The surgeons commented later that they had noticed air entering the grafts during the procedure.

Hypotension at this time may be related to the introduction of nitrous oxide or may be coincidental. It is unlikely to be coincidental, since it happened acutely after the introduction of nitrous oxide and rapidly resolved on its withdrawal. There is some evidence of inherent myocardial depression with nitrous oxide[1] but, usually, cardiac function is well maintained, particularly in patients with previously good left ventricular function. We consider that the most likely explanation is a rapidly expanding air embolism, which caused acute coronary occlusion. An increase in size of air emboli in the presence of nitrous oxide is widely known,[2] as is the risk of systemic emboli with intracranial surgery,[3] laparoscopy,[4] hip replacement[5] and valve surgery.[6] The peroperative introduction of air to the graft is recognised, but we have found no reports of adverse consequences following the introduction of nitrous oxide to the anaesthesia.

Anaesthetists should be aware of this complication since it is probably more common than is recognised.

The London Chest Hospital,
Bonner Road,
London E2 9JX

KATHLEEN M. SHERRY
SUSHEELA SANGWAN

References

1. KAPLAN JA. Cardiac anaesthesia. Volume 2. *Cardiovascular Pharmacology*. Grune and Stratton, 1983.
2. MUNSON ES, MERRICK HC. Effect of nitrous oxide on venous air embolism. *Anesthesiology* 1966; **27**: 783–7.
3. SALE JP. Prevention of air embolism during sitting neurosurgery. The use of an inflatable venous neck tourniquet. *Anaesthesia* 1984; **39**: 795–9.
4. SHULMAN D, ARONSON HB. Capnography in the early diagnosis of carbon dioxide embolism during laparoscopy. *Canadian Anaesthetists' Society Journal* 1984; **31**: 455–9.
5. ANDERSEN KH. Air aspirated from the venous system during total hip replacement. *Anaesthesia* 1983; **38**: 1175–8.
6. LAWRENCE GH, MCKAY HA, SHERENSKY RT. Effective measures in the prevention of intraoperative aeroembolus. *Journal of Thoracic and Cardiovascular Surgery* 1971; **62**: 731–5.

Pain with vecuronium

Dr Kumar's observation that the intravenous injection of vecuronium is accompanied by pain (*Anaesthesia* 1985; **40**: 1018) verifies the prediction made here[1] and should be taken into account when using the priming principle.[2] The two factors involved with pain on injection are pH and tonicity. The vecuronium bromide preparation studied (Norcuron, Organon) had a pH of 3.8, which is sufficiently low to produce pain or discomfort on injection and possibly venous sequelae if repeated injections are given. It should be pointed out, however, that to produce a pharmaceutical preparation with a satisfactory pH and isotonic is not a simple task. Often, unfortunately, a degree of pharmaceutical completeness must be sacrificed in favour of stability and solubility of the active ingredients. The suggestion of Dr Kumar that the manufacturer should supply 2, rather that 1, ml of water-for-injection would not solve the problem. Instead, anaesthetists should adopt a good technique for administering intravenous injections. This should include avoidance of sideports of intravenous cannulae. A slow injection into the giving set of a fast-flowing infusion of, for instance, Ringer's solution is best.

Department of Anaesthesia,
Helsinki University Central Hospital,
00290 Helsinki 29,
Finland

D.A. COZANITIS

References

1. COZANITIS DA. Effects of nondepolarizing neuromuscular blocking agents on erythrocytes in vitro. *American Journal of Hospital Pharmacy* 1984; **41**: 643–4, 648.
2. SCHWARZ S, ILIAS W, LACKNER F, MAYRHOFFER O, FOLDES FF. Rapid tracheal intubation with vecuronium: the priming principle. *Anaesthesiology* 1985; **62**: 388–91.

Delayed 'immediate' bupivacaine toxicity during axillary brachial plexus block

We would like to report a case of delayed toxicity associated with axillary brachial plexus block.

A 64-year-old, 70-kg man with bullous emphysema was admitted for excision of a melanotic lesion of his right index finger. He had been admitted 12 weeks previously with pneumonia and had experienced spontaneous pneumothoraces in the past.

Premedication with papaveretum 20 mg and hyoscine 0.4 mg resulted in satisfactory sedation. A right axillary block was performed after skin infiltration with 1 ml 2% lignocaine. The axillary artery was palpated and fixed against the humerus and the neurovascular sheath was penetrated by a 23-gauge needle anterolaterally to the artery. The patient complained spontaneously of paraesthesia in the hand. After aspiration through a 25-cm electrocath connected to the needle, 30 ml of 0.5 percent bupivacaine were injected. The needle was held steady throughout the injection and manual compression was applied to the upper arm just below the axilla to prevent distal spread of the anaesthetic, as advocated by both Eriksson[1] and Moore.[2]

After 5 minutes, the manual compression was released and within 30 seconds the patient complained of feeling unwell, became restless and rubbed his lips. He then went rigid for 10 seconds with deviation of the eyes to the right. Oxygen was administered and a few seconds later he opened his eyes and complained of feeling strange and uncomfortable. Systolic blood pressure was 70 mmHg and pulse rate 60/minute. The blood pressure increased to 120 mmHg over the next 10 minutes and the patient felt better.

Satisfactory anaesthesia developed in the arm; the operation was carried out and recovery from the anaesthetic was uneventful. The following morning the patient complained of dyspnoea and collapsed shortly after visiting the lavatory. Resuscitation was unsuccessful.

Postmortem examination revealed a large pulmonary embolus in the right lower lobe artery, numerous areas of pulmonary infarction and a deep vein thrombosis of the left calf. Examination of the area of brachial plexus block showed a single pinpoint haemorrhage marking the site of sheath puncture, with no sign of arterial or venous puncture. It would appear that toxic symptoms were not due to inadvertent intravascular injection, although the episode that followed release of upper arm compression exactly mimicked this. There is good evidence that local anaesthetic can enter large intact vessels following paracervical block;[3] it is therefore quite plausible that bupivacaine could have diffused into a relatively empty axillary vein and the bolus effect resulted from venous washout following release of the occluding hand.

This case illustrates a potentially serious source of morbidity in an otherwise well-tolerated procedure. The complication is not mentioned in the standard texts, but we consider that anaesthetists should be aware of it.

Department of Anaesthetics,
St Thomas's Hospital,
Lambeth Palace Road,
London SE1 7EH

J.W. MACKENZIE
J.A. TYTLER

References

1. ERIKSSON E. *Illustrated handbook in local anaesthesia.* 2nd Edn. London: Lloyd-Luke, 1979.
2. MOORE DC. *Regional Block.* 4th Edn. Illinois: Charles C. Thomas, 1973.
3. BEAZLEY JM, TAYLOR G, REYNOLDS F. Placental transfer of bupivacaine after paracervical block. *Obstetrics and Gynaecology* 1972; **39**: 2–6.

Topical adrenaline

It is well known that the intra-operative infiltration of adrenaline is associated with appreciable absorption and the potential for complications.[1] We would like to present a case where the *topical* use of adrenaline was accompanied by potentially serious complications.

A 3-month-old child was anaesthetised with isoflurane, atracurium and the lungs ventilated with 30% oxygen 70% nitrogen and 1% isoflurane, for trabeculectomy for congenital glaucoma. Ten minutes after the start of the procedure, two drops of adrenaline 1% were instilled into one eye. Systolic blood pressure (recorded using an Arteriosonde), which had up until this time been 80–90 mmHg increased to more than 180 mmHg and the patient was peripherally vasoconstricted. Heart rate at this time decreased from 145 to 120 beats/minute. No specific therapy was instituted and the blood pressure gradually returned to 100 mmHg over the next 20 minutes. The patient recovered uneventfully.

It was pointed out that the patient had been receiving similar doses of topical adrenaline to both eyes for some time pre-operatively, apparently without untoward effect. Consequently, it was decided that further adrenaline should be administered, but only with careful monitoring of blood pressure. On ten occasions postoperatively, topical adrenaline (1% one drop to both eyes) was given. Systolic blood pressure was recorded every minute using an EME automatic blood pressure measuring device. On these occasions, systolic pressure increased only by 20 mmHg.

It was established that the child had received 1.5 mg of adrenaline intra-operatively; this is a dose which would not be permitted by local infiltration. Absorption of drugs from the conjunctiva is known to occur; the rate and extent is determined both by the nature of the drug itself as well as local conditions affecting the conjunctiva. Indeed, a similar case has been reported previously, where the intra-operative use of topical phenylephrine (10% solution) during ophthalmic surgery in a child was associated with an increase in systolic blood pressure to 230 mmHg.[2]

We suggest that when unanaesthetised, most of the administered adrenaline rapidly disappears, by crying and eye wiping. This does not occur with drugs given during anaesthesia and all of the administered adrenaline is in a state available for absorption. Caution is advocated when adrenaline is administered to the conjunctival sac during anaesthesia. In addition, it is possible that a reformulation of the adrenaline, perhaps in the form of an ointment, would allow the use of more dilute concentrations of adrenaline to be used with equal efficacy.

Department of Anaesthesia,
Leeds General Infirmary,
Leeds, 1

N.R. WEBSTER
W. HINTON

References

1. GRAY TC, NUNN JF, UTTING JE. *General anaesthesia* Vol 1. 4th Edn London, Butterworths, 1980: 172–3.
2. SOLOSKO D, SMITH RB. Hypertension following 10 per cent phenylephrine ophthalmic. *Anesthesiology* 1972; **36**: 187–9.

Acid aspiration

Dr Crawford[1] remarks that two questions are often raised in discussion about the acid aspiration syndrome: why does it seem to be a lethal event more frequently among obstetric patients than among nonobstetric patients and why did none of the patients in Mendelson's original report die of acid aspiration?

The use of ergometrine during Caesarean section (C-S) may be an aggravating factor in the development of the acid aspiration syndrome, but there are other causes that may play an important role. It is well known that even in well developed countries, where anaesthetic services are well staffed and of high standards, the excellence of care applies almost always only to the surgical ward, the obstetric ward being being the Cinderella, when it comes to anaesthesia equipment and staffing.

It is not uncommon to find hospitals in the United States of America, where obstetric anaesthesia is provided in less than half of the cases by physician anaesthesiologists; the remainder is done by other personnel, obstetric residents, other medical officers, or paramedical personnel (nurse anaesthetists and midwives).[2]

There may be a similar situation in the United Kingdom. The 1976–8 triennial report on Confidential Enquiries into Maternal Mortality in England and Wales, states that 'death was usually due to a combination of inexperience, low general standards of care in labour and in the operating theatre, and poor administrative practices in the form of unskilled assistance or isolation from fully equipped hospitals.[3]

No doubt, the management of vomitus or regurgitation during the induction of a general anaesthetic is handled more adequately by an anaesthesiologist. The Mendelson syndrome, almost a postmortem diagnosis, will be the final result of improper care and inability to make an early diagnosis, and/or to initial mismanagement.

Mendelson's original report was published in 1946, when the standard technique for general anaesthesia consisted of spontaneous breathing, without tracheal intubation. It is well known that artificial ventilation spreads the aspirated gastric contents to the smaller bronchioles and worsens the effect of the acid aspiration. One of the advantages of tracheal intubation is that it protects the airway from aspiration of the vomited or regurgitated gastric contents. This is the reason why the majority of authors advocate the convenience of intubation of every obstetric patient when a general anaesthetic is given. However, this standard practice has not avoided the occurrence of the complication; indeed, in many a case, it has been even worse, because controlled ventilation disseminates the aspirated material even more. It is well known that, in many cases, the possibility of regurgitation and aspiration occurs during induction, following unconsciousness and muscular relaxation, but before insertion of the tracheal tube.[4] In these cases, therefore, the only way to avoid the possibility of death from acid aspiration is to intubate the patient quickly, when this is feasible, and apply artificial ventilation for the shortest possible period of time beforehand.

Another practical aspect of this discussion has led to the so-called difficult intubation drill, to stop attempts at intubation in cases of failed intubation, because these attempts encourage opening of the cardiac sphincter. In these cases, when the operation cannot be delayed, the anaesthetist has to use a facemask with volatile agents, and spontaneous ventilation, just as in the time of Mendelson's report, but with the advantage of the modern halogenated agents for a smooth induction and a prompt recovery.

Leyenda Patria 3118,
P.O. 3,
Montevideo,
Uruguay

S. LIONDAS

References

1. CRAWFORD JS. Ergometrine and death from acid aspiration (Letter). *Anaesthesia* 1985; **40:** 498–9.
2. American College of Obstetricians and Gynecologists 'National Study of Maternity care. Survey of obstetric practice and associated services in hospitals in the United States. A.C.O.G. Chicago, 1971: 25–33.
3. COTTON BR. 'Obstetric anaesthesia'. In: Smith and Aitkenhead, Eds. *Textbook of anaesthesia.* Edinburgh: Churchill Livingstone, 1985: 407.
4. MARX GF. Comment on paper 'Routine endotracheal intubation in obstetrics' *Survey of Anesthesiology* 1970; **14:** 377–8.

Difficult tracheal intubation as a result of unsuspected abnormality of the temporomandibular joint

This is a report of a case who could open her mouth wide pre-operatively but when she was paralysed with neuromuscular relaxants, would not open sufficiently for insertion of the laryngoscope blade. It required a bimanual, forceful and sustained triple airway manoeuvre[1] to establish an adequate opening. However, when relaxed, the jaw retracted vigorously into its locked relaxed position.

The almost-closed mouth permitted only the entry of the finger tips, which were placed posterior to the lower incisors. The mandible was manipulated from within, similar in effect to Safar's modified triple airway manoeuvre by the thumb–jaw lift method.[1] An adequate gap was created to insert the laryngoscope blade which then maintained the jaw forward. Intubation was in fact easy.

Malocclusion was noted pre-operatively, but no significance was attached to it. Subsequent orthodontic assessment showed that the overbite (vertical overlap of the incisors) was severely increased and associated with slightly greater than usual translation (forward gliding) of the condylar head in the glenoid fossa. X-ray of the patients' temporomandibular joints (TMJs) revealed poorly defined and diminutive temporal eminences.

The TMJ is a complex joint,[2] with two compartments separated by an articular disc for biphasic movement. Initial hinge rotation in the lower compartment normally gives ample clearance for the laryngoscope blade. This is followed by translation of the mandibular condyle on the temporal eminence for full opening.

Lateral movement is dependent on differential gliding movement at the two TMJs.

Possible reasons for the difficulty encountered are firstly, the severe overbite, which requires a greater clearance of the incisors, resulted in an inadequate gap during the initial rotation. Secondly, her usually greater translation may mean a greater force is required to open her mouth. Lastly, she may have a tight or extremely elastic posterior ligament (of the joint capsule), normally responsible for spontaneous retraction of the mandible. It is common experience that in some patients, it is difficult to keep the mandible forward without sustained protraction, while others have a lax jaw which is easily protruded to maintain a clear airway.

The state of the TMJ can be affected by malocclusion. Its functional consequence can easily be gauged by the range of movement at the TMJ. It is not obvious whether the patients' abnormality is congenital or secondary to her malocclusion.

It should be the custom to assess mouth opening during the pre-anaesthetic visit. Had this not been done in the above case, the initial inability to open the mouth could have set in train a failed intubation drill unnecessarily. The knowledge that the patient was able to open the mouth adequately made the anaesthetist experiment with various manoeuvres to unlock the TMJs. This confirmed, intubation was eventually an easy procedure. This case also draws attention to the point that some patients do not open their mouths adequately unless the mandible is unlocked or protracted manually.

Department of Anaesthetics, H.K. Tey
Aberdeen Royal Infirmary,
Aberdeen

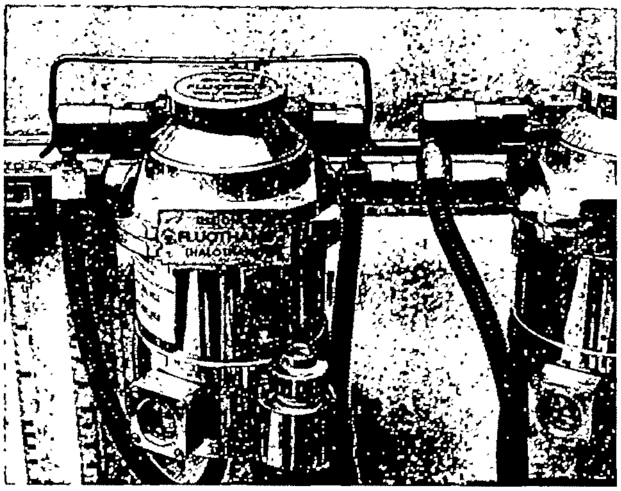
References

1. Safar P. *Cardiopulmonary cerebral resuscitation.* Philadelphia: WB Saunders, 1981.
2. Block C, Brechner VL. Unusual problems in airway management. II. The influence of the temporomandibular joint, the mandible, and associated structures on endotracheal intubation. *Anesthesia and Analgesia* 1971; **50:** 114–23.
3. Posselt U. Physiology of occlusion and rehabilitation. 2nd Edn. Oxford and Edinburgh: Blackwell Scientific Publications, 1968.

A hazard of the Penlon off-line vaporizer mounting system

A recent incident in this department has drawn our attention to a potential hazard of the Penlon off-line vaporizer mounting system.

One of the connecting hoses of the off-line mounting block became partially detached from the vaporizer during the course of an anaesthetic and caused loss of anaesthetic gases from the system. The patient, who had received muscle relaxants, was being maintained on 70% nitrous oxide and enflurane delivered via a Bain system using the Penlon Nuffield 200 ventilator to provide intermittent positive pressure ventilation. The patient received only oxygen from the ventilator and had a greatly increased dead space as a result of the leak. There was, however, only a small loss of tidal volume and it was the signs of inadequate anaesthesia which led to the detection of the problem. The fault was then rapidly corrected and the remainder of the anaesthetic was uneventful. The patient later complained of awareness but not pain during the course of the surgical procedure. There were no other ill effects.



The anaesthetic machine had been carefully checked before use and at that time no leak had been present. The final part of the test involved using the oxygen flush and it is thought that the back pressure exerted on the system by this may have been enough to dislodge the connexion. Subsequent tests have shown that this is possible, although it does require the connectors already to be slightly loose.

The design of the Penlon off-line mounting system with the connexions without positive locking mechanism will always present a potential hazard. Inadvertent disconnexion is particularly likely to occur when the anaesthetic machine is being moved around in the operating room. Loss of fresh gas flow would normally be detected promptly because of collapse of the reservoir bag or failure of a minute volume divider type of ventilator. This is not true when the Bain system and Penlon Nuffield 200 ventilator is used and extra vigilance is requred.

We have devised a simple clip which can be fitted over the off-line mounting connectors (Fig. 1), in order to prevent repetition of this accident. This not only ensures that spontaneous disconnexion will not take place, but also provides a visual confirmation of the integrity of the connexion. Different sizes of clip are required for different designs of vaporizer, but they are simple and inexpensive to make. We have discussed this problem with the manufacturers and they have indicated that a similar clip will be made available commercially.

Department of Anaesthetics,
Northampton General Hospital,
Northampton.

R.H.K. Marsh
N.F. Thomas

Survey on breathing system disconnexions

In January 1984 the Association of Anaesthetists of Great Britain and Ireland circulated to its members a questionnaire on accidental disconnexions in breathing systems. The questionnaire, prepared by the Bureau of Medical Devices of Health and Welfare Canada, was intended to compare the experiences and opinions of anaesthetists in the United Kingdom with those of their Canadian counterparts surveyed in 1983 with the collaboration of the Canadian Anaesthetists' Society.[1]

The response rate in the survey (2.5% members) was too low to draw reliable statistical conclusions, but we would like to report qualitatively on the results. Both the Canadian and British surveys showed that accidental disconnexions are very common. However, because they are usually detected before harm comes to the patient, most anaesthetists have come to accept them and no longer regard them as an equipment fault. Both surveys gave almost identical results for the overall frequency of disconnexions, a median value of four per hospital per year.

The three sites at which disconnexions occurred most often were, in order of frequency, the tracheal tube, the common gas outlet and the ventilator delivery hose. About half of the respondents use some sort of antidisconnect mechanism, most often adhesive tape. Fifty-seven percent use antidisconnect alarms during ventilation of the lungs. The use of alarms was one of the few major differences between British and Canadian practice: 87% of Canadian anaesthetists we surveyed reported using disconnect alarms.

Although the majority of respondents agreed that the problem of disconnexions is due primarily to inadequate design of the connectors, there were differences of opinion about the best solution. Many believed that improved connectors, perhaps with locking mechanisms, are urgently needed. However, about a quarter of respondents believed that antidisconnect devices are unnecessary, because an anaesthetist's 'duty of care' demands careful attention to the patient at all times. A few actually stated that the use of antidisconnect devices would be hazardous, since it would encourage a false sense of security and a relaxation of attention. The fact that so few of the many accidental disconnexions result in harm to the patient is a tribute to the vigilance of anaesthetists. However, improvements in connector design should not be neglected on the grounds that the risk of disconnexions is beneficial as an encouragement to that vigilance.

An argument often cited against the use of antidisconnect devices is that they would lead to an increase in the number of accidental extubations due to the elimination of a mechanical 'fuse' in the system. We believe that this is not a valid argument. A tracheal tube connector should not be expected to serve as a strain relief. The force necessary to pull apart a properly assembled 15-mm connector is itself more than enough to cause extubation. Furthermore, many anaesthetists tape the tracheal connector, thereby defeating its role as a mechanical fuse.

In an age of high technology medicine, conical connectors are incongruous anachronisms. Few areas of industry or transportation would tolerate such notoriously unreliable components in a safety or life support system. Perhaps the major reason that technical solutions to the problem of disconnexions have been slow in coming is that the medical profession has not demanded them. Device manufacturers have produced several workable designs for locking connectors and others are under development. Their acceptance by the profession will depend on a decision by anaesthetists not to regard the nuisance and hazard of accidental disconnexions as unavoidable.

Bureau of Medical Devices, P.D. Neufeld
Environmental Health Centre, Elizabeth A. Walker
Tunney's Pasture, D.L. Johnson
Ottawa, Ontario,
Canada
K1A0L2

Reference

1. Neufeld PD, Johnson DL. Results of the Canadian Anaesthetists' Society opinion survey on anaesthetic equipment. *Canadian Anaesthetist's Society Journal* 1983; **30:** 469–73.

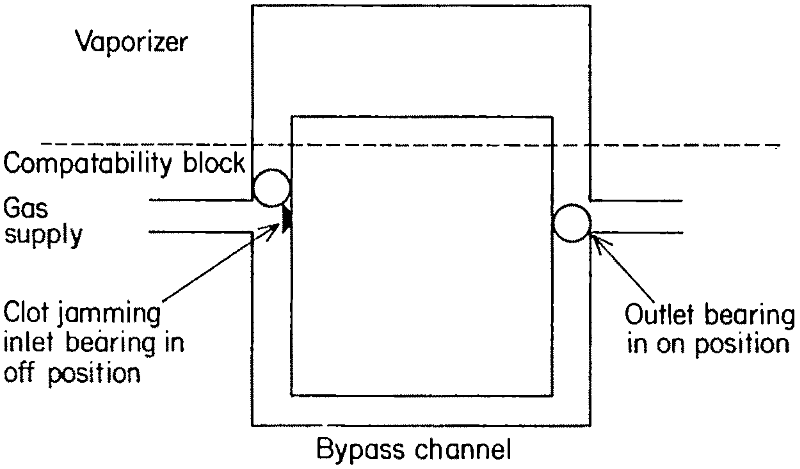
Selectatec system: misplaced blood

We would like to report a potentially serious incident which involved the Ohmeda Selectatec System. Isoflurane is frequently administered during cardiopulmonary bypass from a Tec 4 vaporizer with a compatibility block mounted on the pump machine. When the vaporizer was turned on, no bubbling occurred in the oxygenator; when the vaporizer was removed from the compatibility block, gas flow resumed. No fault was found in the vaporizer.

When the compatibility block was dismantled, an imperfection in the moulding of the lower seat of the inlet port valve was found. Sitting on this defect was a small clot of blood which prevented proper seating of the valve bearing. Thus, in the off position, the gas supply by-passed the vaporizer normally. When the vaporizer was switched on, the gas supply was prevented from entering the vaporizer by the malfunctioning inlet valve and could not flow through the bypass channel due to the normal operation of the outlet port valve (Fig. 1).

It is suggested that when the vaporizer is removed from a Selectatec compatibility block, care should be taken to prevent contamination of the manifold port valves with debris.

Royal Liverpool Children's Hospital, J.M. Goddard
Myrtle Street, T.R. Abbott
Liverpool L7 7DG


Vaporizer
Compatability block
Gas supply
Clot jamming inlet bearing in off position
Outlet bearing in on position
Bypass channel

Two unilateral epidural blocks

We would like to report the unusual management of a case of unilateral epidural block which supports the concept of a dorsomedian septum dividing the epidural space.

One of us (RM) set up an epidural for the treatment of mild hypertension and the relief of labour pain for a 25-year-old woman with an intra-uterine death. An 18-gauge cannula was inserted at the L_3-L_4 interspace, with the patient in the left lateral position. Administration of a total of 15 ml bupivacaine 0.25 percent resulted in a right-sided block. Four further doses were administered with no improvement, despite withdrawal of the cannula by one centimetre. Thirteen hours after the cannula was inserted, the patient was still in labour and in some distress, despite two doses of intramuscular morphine 10 mg.

The other author (GN) was asked to see her. She had bilateral pain and it was considered that her particular situation merited complete analgesia. A second epidural puncture was performed at the L_2-L_3 interspace, with the Tuohy needle directed to pierce the interlaminar ligament to the left of the midline. A second cannula was inserted and 9 ml lignocaine 1 percent injected. This produced effective analgesia on the left side only. Injection of 5 ml bupivacaine 0.25 percent through the original cannula produced the desired effect of complete analgesia and a very grateful patient.

We are not aware of any earlier reports of dual epidural cannulation for unilateral block. We are aware of only one potential complication: the severance of the original cannula by the second needle. In this case there were 9 cm of cannula in the patient and it was considered that there were between 3.5 and 4.0 cm in the epidural space. For the second procedure, the needle was angled to traverse the interspinous space at as cephalad an angle as possible. It was our intention to continue the epidural block by giving increments of 4 ml bupivacaine 0.25 percent to each side, but in the event this was unnecessary as the labour progressed to delivery shortly after the full block was established.

If a more cautious spacing of two rather than one intervertebral space were used, we feel that such a technique could offer the best course of management of this problem.

Walsgrave Hospital, G. NUNN
Clifford Bridge Road, R.P.G. MACKINNON
Walsgrave, Coventry CV2 2DX

Premedication for children

Dr Padfield's comparison of temazepam and trimeprazine for the premedication of children having minor ENT surgery was interesting. (*Anaesthesia* 1985; **40:** 1138). What I found surprising was that it was considered acceptable to proceed with an anaesthetic induction in the 12 and 16% respectively, of patients who were crying and struggling, that is they required to be held down by force, for the anaesthetic to be given. Induction was presumably by mask, since it is virtually impossible to perform an intravenous induction on a struggling child.

Adrian While, a consultant ophthalmologist, recently commented about an anaesthetic given to his own 3-year-old daughter for a similar operation and evoked considerable sympathy in the subsequent correspondence.

Minor ENT surgery is hardly of a life and death nature, and I would suggest that, when a child is so terrified that anaesthesia can only be induced during physical restraint, humanitarian considerations ought to result in the case being postponed until after a more substantial premedication has been given. Better still, of course, would be to give this more substantial premedication in the first place. Gray and Nunn state that papaveretum 0.4 mg/kg and hyoscine 0.008 mg/kg is probably the best for children.

I cannot remember any child crying or struggling after this premedication in the many years in which I have used it. Additionally, venepuncture is well tolerated, even when two or three attempts are required; thus, one avoids the unpleasantness of the mask and children are alert enough to go home the same day. Children do not object to injection half as much as is commonly supposed (I frequently do my own), and this is, I suspect, a myth which originates from the nursing staff.

Dr While makes a plea that it is time we examined and changed our widespread methods of paediatric anaesthesia. In this day and age, no adult would tolerate being held down to be given an anaesthetic. Is it not time that someone spoke up for the children?

North Staffordshire Hospital Centre, A.J. CARTER
City General Hospital,
Newcastle Road,
Stoke-on-Trent ST4 6QG

Reference

1. WHILE A. Personal View. *British Medical Journal* 1985; **291:** 343.

Apparent postoperative recurarisation

We are currently investigating the use of muscle relaxants during cardiac surgery, associated with hypothermic, (30°C), cardiopulmonary bypass. The level of neuromuscular blockade is monitored with a Datex Relaxograph. This measures and records the electromyograph (EMG) of the hypothenar eminence muscles after ulnar nerve stimulation. It was continued until full recovery of neuromuscular function in the intensive care unit.

On several occasions we have noticed a degree of recurarisation after the patient went to the intensive care unit. Figure 1 is the trace obtained from a patient in whom neuromuscular block was maintained with an infusion of atracurium. The trace covers the period after cardiopulmonary bypass and continues postoperatively into the recovery period. There is a marked decrease in the recorded level of neuromuscular transmission (EMG amplitude) after partial recovery of neuromuscular function. This change in EMG amplitude correlated with a decrease in the patient's peripheral

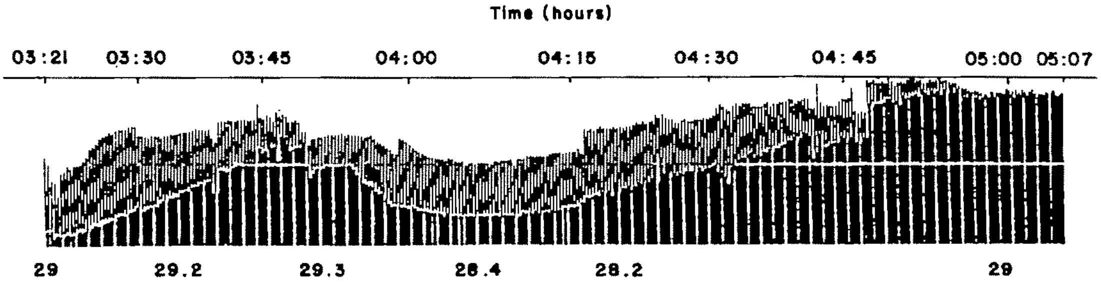


Fig. 1. Hypothenar muscle EMG amplitudes in response to train of four ulnar nerve stimulation. (T1-light, T4-heavy), demonstrating a decrease in amplitude as the peripheral temperature fell from 29.2–28.4°C.

temperature, although the core temperature remained constant. This effect could be predicted from previous work on neuromuscular transmission and temperature,[1] which showed that acetycholine release was reduced by hypothermia in experimental animals and man.

The clinical significance of the observation is that there may be a discrepancy between respiratory muscle power as assessed by respiratory effort and peripheral transmission as assessed by ulnar nerve stimulation at the wrist.

Department of Anaesthetics,
Papworth Hospital,
Papworth Everard,
Cambridge CB3 8RE

N.M. Denny
D.W. Bethune,
I. Hardy
J.D. Kneeshaw
R.D. Latimer

References

1. Thornton RJ, Blakeny C, Feldman SA. The effect of hypothermia on neuromuscular conduction. *British Journal of Anaesthesia* 1976; 48: 264.
2. Churchill-Davidson HC. In *A practice of anaesthesia* 5th edn. Ch. 24 London: Lloyd Luke, 1984: 720–2.

Oculocardiac reflex from the empty orbit

Reflex cardiac dysrhythmias are well known to occur during ocular surgery, where the commonest manifestation is sudden severe bradycardia resulting from pressure on the eyeball or traction on the extra-ocular muscles.

We would like to report the occurrence of the oculocardiac reflex in a patient undergoing excision of a huge, haemorrhagic left peri-orbital tumour. Our patient was a 66-year-old male; the tumour was diagnosed as a moderately well differentiated squamous cell carcinoma. The growth measured 18 × 10 × 6 cm and CT scan revealed complete destruction of the left eye and its orbital floor. The tumour extended to the maxillary and ethmoidal sinuses and the nasal septum. There was no intracranial extension, but nasopharyngeal involvement could not be excluded. Despite the advanced stage of the tumour, systemic screening revealed no distant metastases. On the basis of this finding, plus the fact that the patient required blood transfusions to correct anaemia resulting from frequent brisk haemorrhages from the tumour, surgical excision (simple or radical) was planned. Premedication consisted of oral diazepam 10 mg 2 hours pre-operatively and intramuscular atropine 0.6 mg 45 minutes before surgery. The patient also received 10 mg intravenous diazepam prior to inhalation induction with nitrous oxide, oxygen and halothane mixture. The trachea was intubated and tracheostomy performed with the patient breathing spontaneously.

The patient's lungs were ventilated through the tracheostomy with N_2O O_2 mixture during excision of the tumour; 30 mg tubocurarine and 0.3 mg fentanyl were given at the beginning of the procedure. The electrocardiogram and intra-arterial blood pressure were continuously monitored and induced hypotension was provided with sodium nitroprusside. The heart rate and blood pressure were stable until about 45 minutes after the start of surgery, when the heart rate suddenly showed from 80 to 35 beats per minute and the systolic blood pressure declined from 80 to 30 mmHg. It was observed at this stage that the intra-orbital part of the tumour was being manipulated and excised. Cessation of manipulation followed by 0.6 mg intravenous atropine promptly restored both the blood pressure and the heart rate to their original levels. The rest of the operation proceeded uneventfully.

Previous authors,[1,2] have reviewed the anatomical pathways involved in oculocardiac reflexes. Kerr *et al.*[1] mention the anatomical basis of these reflexes. The occurrence of the reflex in our patient, in whom there was complete destruction of the eye and its socket, supports the view expressed by Kerr that intact ciliary nerves in the orbit could still trigger the oculocardiac reflex in anophthalmic patients.

We would like to suggest that, in addition to ocular surgery, in surgery on the empty orbit, and eyelid surgery in patients with Marcus Gunn Syndrome, oculocardiac reflexes should be anticipated in patients undergoing surgery for peri-orbital tumours, especially if there is orbital involvement. Appropriate monitoring and the well known measures for the prevention of oculocardiac reflexes should therefore be applied to these patients.

Department of Anaesthesia, F. KHAN
King Abdul Aziz University Hospital M.M. ANKUTSE
P.O. Box No. 245 R. MUHJA
King Saud University,
Riyadh 11411,
Saudi Arabia

References

1. KERR WJ, VANCE JP. Oculocardiac reflex from the empty orbit. *Anaesthesia* 1983; **38**: 883–5.
2. KWIK RSH. Marcus Gunn Syndrome associated with an unusual oculocardiac reflex. *Anaesthesia* 1980; **35**: 46–9.

Traumatic nasotracheal intubation

Nasotracheal intubation is a common anaesthetic procedure practised blind. Tubal obstruction by nasal polyp,[1] nasal concha[2] and blood clot[3] have been described. However, the incidence of lesser quantities of tissue and secretions within the tube, collected during its passage through the nose and nasopharynx, is unknown.

Nasotracheal intubation was performed on 100 unselected patients aged 12–79 years, who presented for dental surgery. There were 41 males and 59 females. Pre-operative assessment included an enquiry into previous nasal problems. The relative patency of both nostrils was assessed before induction.[4] The more patent nostril was used for the first attempt at intubation; if they were equal, the right nostril was used first.

Patients were premedicated with papaveretum and hyoscine and anaesthesia induced with thiopentone and suxamethonium. Tracheal intubation was with Magill plain red rubber nasotracheal tubes (Leyland Medical). Size 8.0 mm id tubes were selected for males and sizes 7.0 or 7.5 mm for females. All intubations were carried out by one operator (DCH) and were initially attempted with the head in the 'sniffing the morning air' position and without rotation of the tube.

Nasal passage of the tube was characterised as 'no hold up' if its passage was smooth and required even pressure. 'Hold up' was deemed to occur if there was a noticeable increase in the pressure required to pass the tube or if rotation or other manoeuvre was required.

The tubal lumen was examined following passage into the oropharynx by clockwise rotation of the tube and by elevation and rotation of the tip with Magill forceps when necessary. Soiling was present if a discrete globule of material judged to be more than 2-3 mm in diameter was observed. Data analysis was performed using the Chi squared test.

A 33 percent incidence of soiling was found (Table 1). In seven cases the material looked like adenoidal tissue. All seven cases were associated with bleeding and hold up during passage of the tube. The occurrence of nasal or nasopharyngeal hold up during intubation was associated with an increased incidence of soiling ($p<0.001$), so was the observation of blood at laryngoscopy ($p<0.001$). Indeed, when nasopharyngeal hold up occurred, together with bleeding, there was an 86 percent incidence of soiling. In three of these cases, 50 percent of the tubal lumen was occluded, twice by soft tissue and once by blood clot.

Table 1. Comparison of soiling with hold up and bleeding

	Number of patients	Number of tubes soiled (%)
All cases	100	33 (33)
No hold up	65	13 (20)
Hold up	35	20 (57)*
No bleeding	74	15 (20)
Bleeding	26	18 (69)*
No hold up or bleeding	56	9 (16)
Hold up with bleeding	17	14 (82)

*$p<0.001$.

These results show that soiling is a common occurrence and is a particular problem when hold up during passage into the nasopharynx is accompanied by bleeding. It is not suggested that the technique of blind nasal intubation be abandoned. However, when intubation or throat packing is done under direct vision, consideration should be given to inspection of the tubal lumen prior to intubation.

Department of Anaesthetics, D.C. HARVEY
St George's Hospital, P. AMOROSA
Tooting, SW17 0QT

References

1. BINNING R. A hazard of blind nasal intubation. *Anaesthesia* 1974; **29**: 366–7.
2. BOYSEN K. An unusual case of nasotracheal tube occlusion. *Anaesthesia* 1985; **40**: 1024.
3. HITCHEN JE, WIENER AP. Unexpected obstruction of a nasotracheal tube: report of case. *Journal of Oral Surgery* 1973; 31: 722–4.
4. ATKINSON RS, RUSHMAN KB, LEE JA. *Synopsis of anaesthesia*. 9th Edn: 227.

A case for tonsillectomy

A healthy 4-year-old boy presented for surgical treatment of a hydrocoele under general anaesthesia. He was noted to breathe through his mouth and to have very enlarged tonsils. Anaesthesia was induced with thiopentone and he breathed in 50% N_2/O_2 via a facemask.

It was difficult to maintain a clear airway, so his trachea was intubated. Spontaneous ventilation was allowed throughout the procedure and continued after extubation in the supine position, when the lower jaw was supported. However, when placed in the tonsillar position for transfer to the recovery area, he became peripherally cyanosed, with marked supraglottic airway obstruction. No stridor occurred and it was not possible to relieve the obstruction by pulling the lower jaw forwards or by manual ventilation with a bag and mask.

When he was placed supine again, the obstruction was relieved and satisfactory spontaneous ventilation was possible with only slight support of the jaw. The obstruction returned when he was in the tonsillar position and was only relieved when he was supine. It was now obvious that the enlarged tonsils were the cause and a nasal airway was passed which allowed spontaneous ventilation in the tonsillar position. When this was removed later, he still had some degree of obstruction, but if he lay supine his airway was adequate.

He was referred for an ENT opinion for tonsillectomy, because were he to be rendered unconscious after an accident, he could obstruct his airway if he were placed in the traditional coma (tonsillar) position, with fatal consequences.

Craigavon Area Hospital,
Craigavon,
Co. Armagh BT63 5QQ

R. Cooper

Intra-articular bupivacaine for pain relief in arthroscopic surgery

The letter by Dr Hughes (*Anaesthesia* 1985; **40:** 821) is interesting. Whereas I cannot dispute the statistically significant superiority of his technique of femoral nerve block over intra-articular bupivacaine or postoperative (presumed intramuscular) papaveretum, there are a few points which concern me about this study.

Firstly, it is well documented that complete afferent blockade of the knee joint requires local analgesia of femoral, obturator, and sciatic nerves, although most authorities agree that there is a great deal of individual variation in the proportion contributed by each trunk.[1,2] Dr Hughes' comment that a solitary femoral block should provide complete analgesia for arthroscopic surgery is thus not correct on anatomical grounds.

Secondly, we are given no information on the *technique* of femoral block employed (viz: paravascular single injection, with or without elicitation of paraesthesiae or electrical stimulation, or fan shaped barrage infiltration). If we assume that a paravascular technique was used, employing the volume of bupivacaine stated, it is likely that a lumbar plexus block would occur in a substantial number of cases.[3] The standard volume of local analgesic for isolated femoral block is quoted to be 5–10 ml.[4] If my assumption is correct, then it is not surprising that the results quoted demonstrate superiority of block over the other groups, since both femoral *and* obturator nerves are probably blocked.

Thirdly, Dr Hughes tells us that the Bristol surgeons do not employ vasoconstrictor in their intra-articular injection. Many units, including our own, routinely employ 1/200 000 adrenaline in this type of technique. This would seem a reasonable manoeuvre to reduce absorption of bupivacaine from the inflamed synovium and therefore prolong and intensify the analgesia and also perhaps confer some haemostasis. Two major monographs have recommended the use of a vasoconstrictor, albeit with other local analgesics.[1,4]

Finally, the author does not mention whether his patients were inpatients or day cases. A femoral block (or a lumbar plexus block) is surely contraindicated in day case arthroscopic surgery, because of the inevitable motor blockade which may hamper rapid ambulation postoperatively. It is early mobilisation, made possible by the reduced surgical trauma of an endoscopic technique, which is responsible, in part, for the reduction in postoperative morbidity when compared with an open surgical approach.

Department of Anaesthesia,
Foothills Hospital at the University of Calgary,
1403–29th Street, N.W.,
Calgary, Alberta,
Canada, T2N 2T9

R.J. Eastley

References

1. Moore DC. *Regional block.* 4th Edn. Springfield: Charles C. Thomas, 1975: 281–7, 325–8.
2. Cousins MJ, Bridenbaugh PO. *Neural blockade.* Philadelphia: J.B. Lippincott, 1980: 330–1.
3. Winnie AP, Ramamurthy S, Durrani Z. The inguinal paravascular technic of lumbar plexus anesthesia. The '3-in-1-block'. *Anesthesia and Analgesia* 1973; **52:** 989–96.
4. Eriksson E. *Illustrated handbook in local anaesthesia.* Philadelphia: W.B. Saunders, 1980: 106–7, 149–50.

Power failure in an intensive care unit

The intensive care unit at Gloucester Royal Hospital recently experienced a total power cut when the mains supply cable to the block shorted out. The unit was suddenly plunged into complete darkness, with failure of all monitors, ventilators and infusion pumps. At the time there were six patients on the unit, four of them on ventilators and two dependent upon inotropic support. Attempts to sort out the situation in a calm and orderly manner were not aided by the clangour of four electronic ventilator and seven infusion pump alarms and the agitation of visiting relatives. Power was restored after seven minutes and, fortunately, all the patients survived the experience without harm.

The incident, however, emphasised several important points. Firstly, the need for one nurse to be present in the unit at all times for each ventilated patient. Secondly, the need for an alternative manual method of ventilation which does not require reconnexion of pipelines or flowmeters. Re-organisation of the gas supplies would have been impossible in the darkness. Thirdly, some auxillary form of lighting must be available. There was no built-in emergency lighting in the ward and one of the two available torches had a broken bulb. Finally, it is wise to ensure that when patients are dependent upon inotropic support or hypotensive agents, the infusion pumps supplying these drugs should have battery back-up.

Gloucestershire Royal Hospital,
Gloucester, GL1 3NN
C.J.H. Johnson

Unpredictable spread of heavy cinchocaine

With reference to the letter from Drs Bembridge, Macdonald and Lyons (*Anaesthesia* 1985; **40:** 1018), I have seen two cases of an unpredictable and patchy block following spinal anaesthesia for Caesarean section. Both were routine spinals performed in the left lateral at the L_{2-3} interspace and both had a high (T_1) and low (S_{3-4}) level without a surgical block between. This was attributed to the anaesthetic being introduced at the apex of the accentuated lumbar lordosis seen in these patients.

Without knowing more details of the technique used by the above authors, specific conclusions cannot be reached, but an accentuated lumbar lordosis may cause a rapid pooling of heavy local anaesthetic solutions and this may result in poor and unpredictable block unless the patient has such a curvature reduced at the time, using accepted techniques.

Department of Anaesthetics,
Scunthorpe General Hospital,
Cliff Gardens,
Scunthorpe,
South Humberside
C.A. Moore

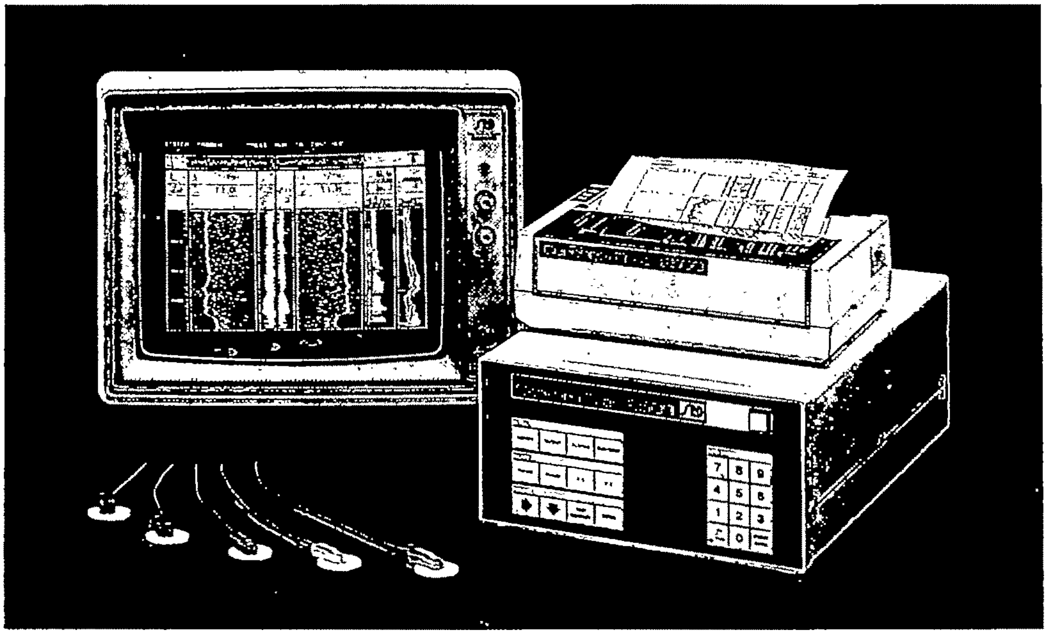
The use of a biopsy brush wire as a bronchoscope guide

The fibreoptic bronchoscope/laryngoscope is being increasingly used in cases of difficult intubation. One disadvantage of the system is that the bronchoscope has to be preloaded with the appropriate sized tracheal tube. Recently, when using this method in a patient with rheumatoid arthritis, great difficulty was experienced in finding, and entering, the larynx. It was then found that the tube was too large to enter into the trachea, probably as a result of three previous elective tracheostomies. A bronchial cytology brush wire was passed via the side channel of the bronchoscope into the trachea and the bronchoscope removed, leaving the wire in place. The bronchoscope was then loaded with a smaller tracheal tube and the bronchoscope re-introduced without difficulty, using the wire as a guide. The intubation was then completed without difficulty.

This system could usefully be employed in cases of difficult intubation, where the appropriate size of tracheal tube is unknown, for example where there has been previous tracheal surgery or in paediatric practice.

Department of Anaesthetics,
Cardiothoracic Unit,
Northern General Hospital,
Sheffield S5 7AU
S.P. Gerrish
G.A. Weston

CEREBRO·TRAC 2500



FULL CEREBRAL STATUS AT A GLANCE

- Depth of Anaesthesia Monitoring
- Vascular and Cardiac Surgery
- Critical Care Monitoring

CEREBRO-TRAC's unique, easy-to-read display format presents you with a trended Density Spectral Array from 2 channels of EEG, plus up to 4 related physiological parameters, on a single VDU screen.

This integrated at-a-glance display gives you the complete picture (real-time status and trends) ensuring rapid alert and response to early signs of cerebral hypoxia, ischemia and changes in anaesthetic depth.

The last word in cerebral monitoring, CEREBRO-TRAC is fully compatible with your existing monitoring equipment and designed to keep pace with future developments.

All this in a single integrated display:

- Real-Time EEG Waveforms
- Trended Density Spectral Array of FFT Processed EEG.
- Trended Display of Spectral Edge Frequency
- Trended EEG Amplitude
- Trended Display of Frontalis Muscle Activity
- Trended Displays of 4 other user-selected Parameters (Heart Rate, Blood Pressure, CO_2, O_2, Temperature etc.)
- Alarms and Event Markers

PLUS digital real-time values of all the above displayed parameters

Contact us now for a demonstration

NEUROSCIENCE LTD NEURO HOUSE, 1 ST JAMES ROAD, BRENTWOOD,
ESSEX, ENGLAND. TELEPHONE: 0277 230909
In the USA: Neuroscience Inc., 210 Topaz Street, Milpitas, CA. 95035, USA.

7th EUROPEAN CONGRESS OF ANAESTHESIOLOGY

VIENNA 7-13 September 1986

Austria is a beautiful country and there is no better time to visit than early September.
Vienna is one of Europe's magnificent capitals boasting the Imperial Palace, the Hofburg (surely one of the world's most beautiful conference centres), the River Danube, the Opera, Spanish Riding School, not to mention the music of Strauss, Mozart and Beethoven.

Fishley Sebley have prepared a travel programme which includes the fantastic *Venice Simplon Orient-Express,* special delegate flights, and magnificent hotels. Post Congress tours will include visits to the 'Lake District' near Velden, and Budapest.

For Travel Brochure Contact:

Fishley Sebley

Fishley Sebley Associates (Travel) Ltd
4 Lower Belgrave Street
London SW1W 0LJ
Telephone 01-730 8241
Telex 918450 FISSEB G

A problem with Murphy's eye

The design of several polyvinylchloride tracheal tubes includes a fenestration near to the tip (Murphy's eye), which allows ventilation to the right lung even when the tube is placed too close to the carina. This fenestration may lead to problems when Magill forceps are used during nasotracheal intubation. When the tip of the tube is grasped between the jaws (the cuff area is avoided to prevent inadvertent puncture of the cuff) and passed into the larynx, the tip of one arm of the forceps may slip through Murphy's eye and become lodged, which necessitate manoeuvres to distangle the two. This can result in both laryngeal damage and inadequate ventilation during this period.

In order to avoid this, an alternative method of nasotracheal intubation would be to insert the nasal tube as far as the oropharynx, pass a long (40 cm) reinforced plastic introducer through the lumen, to lie just proximal to the larynx, and then, using Magill's forceps as necessary, manoeuvre the introducer through the cords before the tracheal tube is passed over it into the larynx.

Newcastle General Hospital,
Westgate Road,
Newcastle upon Tyne NE4 6BE
J.F. HARRISON

Spinals

There was a saying before the advent of general anaesthesia that the kind surgeon warms his knife prior to cutting; today it would be appropriate to paraphrase it to the kind anaesthetist warms his needle (and cleansing lotion) prior to injection.

The cleansing solutions and needles used for regional anaesthesia are normally stored in the anaesthetic room and are, therefore, about 20°C cooler than body temperature. A cold cleansing lotion applied to the skin startles the patient, with the result that the muscles tense and, thus, the carefully arranged position is lost. Keeping the cleansing solution in the theatre warming cabinet would solve this problem and would be appreciated by the patient.

Cold needles affect cerebrospinal fluid (CSF) temperature and thus, when a spinal subarachnoid block is performed using a fine (25 G) spinal needle inserted through an introducer, the first 0.5 ml of aspirated CSF feels cold when it is tested on the operator's forearm. Initially, I thought that this observation would invalidate the differential temperature test between CSF and saline used to localise the epidural space. However, if a wide bore spinal (or epidural) needle is used, or if the introduction of a fine spinal needle through the introducer takes time to reach the subarachnoid space, then the needle is warmed by the patient's tissues and the ensuant CSF feels warm. The only useful application of this observation is to propound the law that 'the skill of the subarachnoidist using a needle and introducer is inversely proportional to the temperature of the ensuant CSF'.

Keeping the needles in a warming cabinet would invalidate this law, while keeping them in a refrigerator would not provide a true reflection of skill.

District General Hospital,
Colchester, CO4 5JL
F.F. CASALE

Rational metric doses of anticholinergic drugs

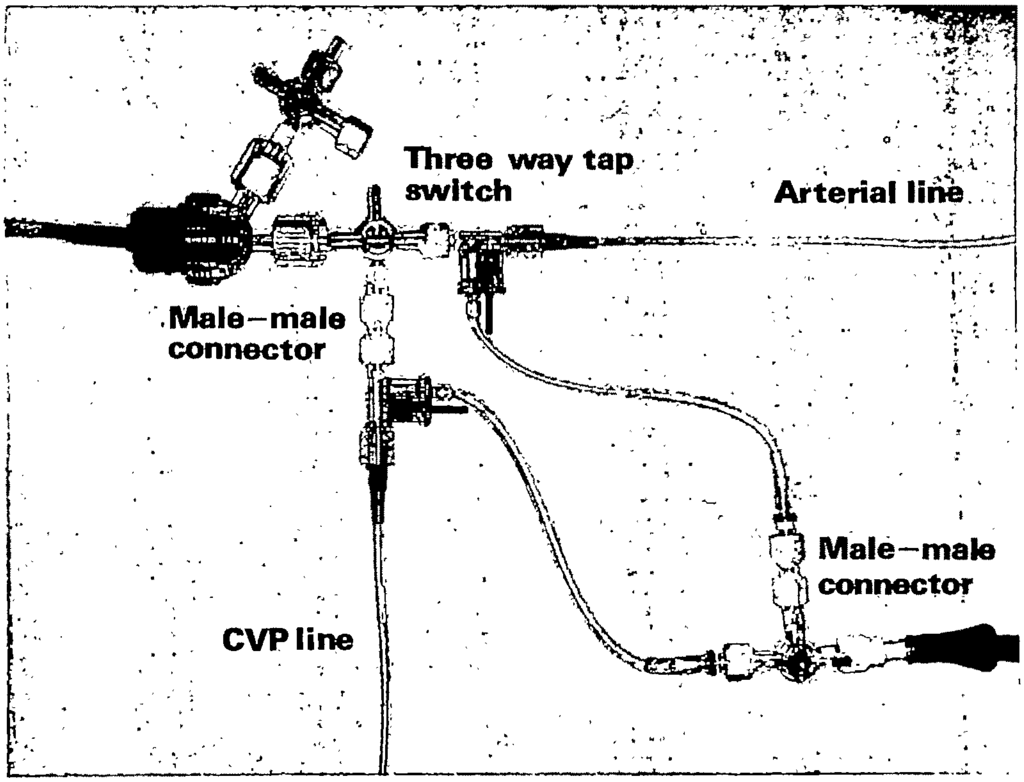
Dr Mirakhur (*Anaesthesia* 1985; **40:** 1139) has commented on the odd doses of atropine we use. Atropine *is* available in ampoules containing 0.5 mg of the drug. We have used the preparation from Antigen for several years now. Calculation of paediatric doses is much easier than with the old 1/100 grain ampoules.

Queen Mary's Hospital For Children,
Carshalton,
Surrey, SM5 4NR
P. RADFORD

A further modification for direct arterial and central venous pressure monitoring

Further to the letter by Dr Wilson (*Anaesthesia* 1985; **40:** 711) about combined central venous and direct arterial pressure monitoring, we describe a further simplification of this method, in which one tap only need be adjusted.

The direct arterial and central venous pressure lines are both connected, via their Intraflos, to a three-way tap, using a male–male connector on the central venous pressure line. To monitor arterial pressure, the central three way tap, or 'switch tap', is put to the position shown in the figure. To change to central venous pressure monitoring, all that is needed is a turn of the 'switch



tap' 90° anticlockwise; this simultaneously shuts off the arterial pressure monitoring.

This simple modification is an improvement.

Anaesthetic Department,
Queen Victoria Hospital,
East Grinstead,
West Sussex RH19 3DZ

N.C. Huddy
Alice Gaynor

Anaesthesia, 1986, Volume 41, pages 447–453

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for October 1985. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Abdominal surgery

Vasoactive agents in control of the mesenteric circulation. BANKS, R.O., GALLAVAN, R.H. *et al. Federation Proceedings* 1985; **44:** 2743.

Action of agonists and antagonists at muscarinic receptors present on ileum and atria *in vitro*. CLAGUE, R.U., EGLEN, R.M. *et al. British Journal of Pharmacology* 1985; **86:** 163.

Red for danger: blood transfusion and colorectal cancer. FIELDING, L.P. *British Medical Journal* 1985; **291:** 841.

Vasoactive agents and the mesenteric microcirculation. HARPER, S.L., BOHLEN, G.H., GRANGER, D.N. *American Journal of Physiology* 1985; **249:** G309.

Intestinal blood flow (Editorial). QAMAR, M.I., READ A.E. *Quarterly Journal of Medicine* 1985; **56:** 417.

Comparative hemodynamic effects of selective superior mesenteric arterial and peripheral intravenous glucagon infusions. WRIGHT, C.D., KAZMERS, A. *et al. Journal of Surgical Research* 1985; **39:** 230.

Pharmacology

Adrenergic drugs and their antagonists

Beta-blockers and sleep—a controlled trial. BETTS, T.A., ALFORD, C. *European Journal of Clinical Pharmacology* 1985; **28:** 65.

A possible central action of prazosin and ketanserin to cause hypotension. COPELAND, I.W., BENTLEY, G.A. *Journal of Cardiovascular Pharmacology* 1985; **7:** 822.

Beta-blocking concentrations in man. CRUICKSHANK, J.M., NEILDWYER, G. *European Journal of Clinical Pharmacology* 1985; **28:** 21.

No evidence for differences between pre- and post-junctional beta 2-adrenoceptors. DOCHERTY, J.R., HYLAND, L. *British Journal of Pharmacology* 1985; **86:** 335.

Measurement of plasma catecholamine concentrations—an assessment of anxiety. FELL, D., DERBYSHIRE, D.R. *et al. British Journal of Anaesthesia* 1985; **57:** 770.

Adrenergic receptors: molecular mechanisms of clinically relevant regulation. LEFKOWITZ, R.J., CARON, M.G. *Clinical Research* 1985; **33:** 395.

Intrinsic sympathomimetic activity of cardio-selective beta-adrenoceptor blockers and effects on renal function. MACKAY, I.G., MACNICOL, A.M. *et al. British Journal of Clinical Pharmacology* 1985; **20:** 197.

Anaesthetic agents

Dose dependent pharmacokinetics of midazolam. BORNEMANN, L.D., MIN, B.H. *et al. European Journal of Clinical Pharmacology* 1985; **29:** 91.

Hyperbaric pressure of 51 atmospheres is without effect on the depression of oxygen uptake in kidney tissue culture produced by halothane. COHEN, P.J., BEDOWS, E. *et al. Life Sciences* 1985; **37:** 1221.

Etomidate versus thiopental for induction of anesthesia. GIESE, J.L., STOCKHAM, R.J. *et al. Anesthesia and Analgesia* 1985; **64:** 871.

Effect of transdermal scopolamine on salivation. GORDON, G., BEN-ARYEH, H. *et al. Journal of Clinical Pharmacology* 1985; **25:** 407.

The haemodynamic effects of intravenous induction. Comparison of the effects of thiopentone and propofol. GROUNDS, R.M., TWIGLEY, A.J. *et al. Anaesthesia* 1985; **40:** 735.

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London, WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. An exact copy of the monthly section or various cumulative classifications of the Anaesthetic Literature published in the Journal can be obtained on application to him. References from January 1984 have been entered on data base and search facilities are also available. All communications about this matter should be addressed to Dr Kaufman please.

Evoked responses—a neurophysiological indicator of depth of anaesthesia (Editorial). SEBEL, P.S., HENEGHAN, C.P., INGRAM, D.A. *British Journal of Anaesthesia* 1985; **57:** 841.

Blocking effect of diltiazem on thiopentone-induced vasoconstriction in isolated canine internal carotid arteries. TSUJI, T., CHIBA, S. *Journal of Cerebral Blood Flow and Metabolism* 1985; **5:** 446.

Effects of diazepam at the neuromuscular junction. WALI, F.A. *Life Sciences* 1985; **37:** 1559.

Cerebrovascular adaptation to prolonged halothane anesthesia is not related to cerebrospinal fluid pH. WARNER, D.S., BOARINI, D.J., KASSELL, N.F. *Anesthesiology* 1985; **63:** 243.

Analgesic agents

Comparison of the cardiovascular effects of meptazinol and naloxone following haemorrhagic shock in rats and cats. CHANCE, E., PACIOREK, P.M. *et al. British Journal of Pharmacology* 1985; **86:** 43.

Clinical assessment and plasma pharmacokinetics associated with intramuscular or extradural alfentanil. CHAUVIN, M., SALBAING, J. *et al. British Journal of Anaesthesia* 1985; **57:** 886.

Opiate antagonist W1N44, 441-3 stereospecifically improves neurological recovery after ischemic spinal injury. FADEN, A.I., JACOBS, T.P. *Neurology* 1985; **35:** 1311.

Pharmacokinetics of phenoperidine in anaesthetized patients undergoing general surgery. FISCHLER, M., LEVRON, J.C. *et al. British Journal of Anaesthesia* 1985; **57:** 872.

Severe hypertension induced by naloxone. LEVIN, E.R., SHARP, B. *et al. American Journal of Medical Science* 1985; **290:** 70.

Naloxone does not modify the hemodynamic and neuroendocrine effects of clonidine in normal humans. PEDRINELLI, R., BERNINI, G.P., SALVETTI, A. *Journal of Cardiovascular Pharmacology* 1985; **7:** 953.

Variability of fentanyl pharmacokinetics in man. Computer predicted plasma concentrations for three intravenous dosage regimens. REILLY, C.S., WOOD, A.J.J., WOOD, M. *Anaesthesia* 1985; **40:** 837.

Adverse effects due to morphine sulfate. Challenge to previous clinical doctrine. SEMENKOVICH, C.F., JAFFE, A.S. *American Journal of Medicine* 1985; **79:** 325.

Naloxone inhibits superoxide release from human neutrophils. SIMPKINS, C.O., IVES, N. *et al. Life Sciences* 1985; **37:** 1381.

Naloxone does not prevent death after rapid hemorrhage in swine. TRAVERSO, L.W., BELLAMY, R.F., OBENAR, J.D. *Surgery Gynecology and Obstetrics* 1985; **161:** 229.

Antagonism of fentanyl and alfentanil by intravenous plus subcutaneous naloxone. Pattern of ventilatory depression after a short procedure. VALGARDSSON, A., WERNER, O., SVENSSON, G. *Anaesthesia* 1985; **40:** 772.

Muscle relaxants

The potencies of edrophonium and neostigmine as antagonists of pancuronium. BREEN, P.J., DOHERTY, W.G. *et al. Anaesthesia* 1985; **40:** 844.

Vecuronium in the myasthenic patient. HUNTER, J.M., BELL, C.F. *et al. Anaesthesia* 1985; **40:** 848.

The use of different doses of vecuronium in patients with liver dysfunction. HUNTER, J.M., PARKER, C.J.R. *et al. British Journal of Anaesthesia* 1985; **57:** 758.

Response differences of paretic and healthy extremities to pancuronium and neostigmine in hemiplegic patients. IWASAKI, H., NAMIKI, A. *et al. Anesthesia and Analgesia* 1985; **64:** 864.

Modification by dantrolene, procaine and suxamethonium of caffeine-induced changes in aequorin luminescence transients and twitch tensions. KIMURA, I., KIMURA, M., KIMURA, M. *British Journal of Pharmacology* 1985; **86:** 319.

Relation between electromyogram and force in fatigue. KRANZ, H., CASSELL, J.F., INBAR, G.F. *Journal of Applied Physiology* 1985; **59:** 821.

A comparison of edrophonium and neostigmine for the antagonism of atracurium-induced neuromuscular block. LAVERY, G.G., MIRAKHUR, R.K., GIBSON, F.M. *Anesthesia and Analgesia* 1985; **64:** 867.

Atacurium and intraocular pressure. MURPHY, D.F., EUSTACE, P. *et al. British Journal of Ophthalmology* 1985; **69:** 673.

Influence of tubocurarine, pancuronium and atracurium on bronchomotor tone. SIMPSON, D.A., WRIGHT, D.J., HAMMOND, J.E. *British Journal of Anaesthesia* 1985; **57:** 753.

Assessment of neuromuscular blockade produced by atracurium in frog sartorius muscle. WALI, F.A. *Pharmacological Research Communications* 1985; **17:** 711.

Other drugs

Cholinergic properties of choline ethers. CHATURVEDI, A.K., RAMA SASTRY, B.V. *Archives Internationales de Pharmacodynamie et de Therapie* 1985; **277:** 15.

Pharmacokinetics of ranitidine after intravenous administration in hemodialysis patients. GARG, D.C., BALTODANO, N. *et al. Pharmacology* 1985; **31:** 189.

Clinical significance of esterases in man. WILLIAMS, F.M. *Clinical Pharmacokinetics* 1985; **10:** 392.

Apparatus

Resistance of tracheal tubes 3.0 and 3.5 mm internal diameter. A comparison of four commonly used types. BLOM, H., RYTLANDER, M., WISBORG, T. *Anaesthesia* 1985; **40:** 885.

The clinical value of measuring cardiac output. GEORGE, R.J.D., WINTER, R.J.D. *British Journal of Hospital Medicine* 1985; **34:** 89.

A method for replacement of the endotracheal tube with continuous control of the airway. Halebian, P., Shires, G.T. *Surgery Gynecology and Obstetrics* 1985; **161:** 285.

Oxygen concentrators. Howell, R.S.C. *British Journal of Hospital Medicine* 1985; **34:** 221.

On-line metabolic monitoring of the heart during cardiac surgery. Khuri, S.F., Warston, W.A. *Surgical Clinics of North America* 1985; **65:** 439.

The Newmarket pump: a new suction pump for external negative pressure ventilation. Kinnear, W.J.M., Shneerson, J.M. *Thorax* 1985; **40:** 677.

Validation of a doppler technique for beat-to-beat measurement of cardiac output. Mehta N, Iyawe, V.I. *et al. Clinical Science* 1985; **69:** 377.

Noninvasive doppler determination of cardiac output during submaximal and peak exercise. Shaw, J.G., Johnson, E.C. *et al. Journal of Applied Physiology* 1985; **59:** 722.

Complications

Ischemic brain damage in rats following cardiac arrest using a long-term recovery model. Blomqvist, P., Wieloch, T. *Journal of Cerebral Blood Flow and Metabolism* 1985; **5:** 420.

The pathology of amiodarone neurotoxicity. I. Experimental studies with reference to changes in other tissues. Costa-Jussa, F.R., Jacobs, J.M. *Brain* 1985; **108:** 735.

Carbon monoxide poisoning. Dolan, M.C. *Canadian Medical Association Journal* 1985; **133:** 392.

Cardiac complications following tricyclic antidepressant overdose. Goldberg, R.J., Capone, R.J., Hunt, J.D. *Journal of the American Medical Association* 1985; **254:** 1772.

The pathology of amiodarone neurotoxicity. II. Peripheral neuropathy in man. Jacobs, J.M., Costa-Jussa, F.R. *Brain* 1985; **18:** 753.

Late paraplegia as a consequence of intraaortic balloon pump support. Scott, I.R., Goti, J.J. *Annals of Thoracic Surgery* 1985; **40:** 300.

General anaesthetic procedures

Effect of anaesthetic technique on deep vein thrombosis—a comparison of subarachnoid and general anaesthesia. McKenzie, P.J., Wishart, H.Y. *et al. British Journal of Anaesthesia* 1985; **57:** 853.

Anaesthetic management of the morbidly obese. Robertson, I.K., Eltringham, R.J. *British Journal of Hospital Medicine* 1985; **34:** 224.

Halothane and isoflurane do not decrease Pa_{O_2} during one-lung ventilation in intravenously anesthetized patients. Rogers, S.N., Benumof, J.L. *Anesthesia and Analgesia* 1985; **64:** 946.

General interest

The molecular basis of communication within the cell. Berridge, M.J. *Scientific American* 1985; **253:** 142.

Mean time and first-pass metabolism. Brockmeier, D., Ostrowski, J. *European Journal of Clinical Pharmacology* 1985; **29:** 45.

The many pathophysiologies of sickle cell anemia. Nagel, R.L., Fabry, M.E. *American Journal of Hematology* 185; **20:** 195.

Aging and drug disposition—an update. Schmucker, D.L. *Pharmacological Reviews* 1985; **37:** 133.

The molecular basis of communication between cells. Snyder, S.H. *Scientific American* 1985; **253:** 132.

Sarcoidosis and its neurological manifestations. Stern, B.J., Krumholz, A. *et al. Archives of Neurology* 1985; **42:** 909.

The therapeutic system—therapeutic implications of rate controlled drug delivery. Urquhart, J. *Directed Drug Delivery*. Ed: RT Borchardt *et al.* 1985: Humana Press (Clifton): 51.

Local analgesia

Kinetics of cocaine distribution, elimination and chronotropic effects. Chow, M.J., Ambre, J.J. *et al. Clinical Pharmacology and Therapeutics* 1985; **38:** 318.

Spinal and epidural analgesia

Plasma concentrations of lidocaine and its principal metabolites during intermittent epidural anesthesia. Inoue, R., Suganuma, T. *et al. Anesthesiology* 1985; **63:** 304.

Spinal cord blood flow following subarachnoid lidocaine. Kozody, R., Swartz, J. *et al. Canadian Anaesthetists' Society Journal* 1985; **32:** 472.

Spinal opioids

Morphine concentration in brain and spinal cord after subarachnoid morphine injection in baboons. Gregory, M.A., Brocke-Utne, J.G. *et al. Anesthesia and Analgesia* 1985; **64:** 929.

Opioid control of the function of primary afferent substance P fibres. Lembeck, F., Donnerer, J. *European Journal of Pharmacology* 1985; **114:** 241.

Obstetric anaesthesia and analgesia

Thermal injury to pregnant patient. Amy, B.W., McManus, W.F. *et al. Surgery Gynecology and Obstetrics* 1985; **161:** 209.

Intracellular electrolytes and efflux kinetics in pregnancy-induced hypertension. Bramley, P.M., Miller, J.A., Wilson, P.D. *Proceedings of the University of Otago Medical School* 1985; **63:** 34.

Fetal heart rate decelerations after oxytocin infusion in an abdominal pregnancy. Cabbad, M.F., Minkoff, H., Faustin, D. *Obstetrics and Gynecology* 1985; **66:** S2.

Evaluation of the pharmacodynamics and pharmacokinetics of ritodrine when administered as a loading dose. Caritis, S.N., Li, S.L., Wong, L.K. *American Journal of Obstetrics and Gynecology* 1985; **152:** 1026.

Preeclampsia eclampsia—hemodynamic and neurologic correlations. Clark, S.L., Divon, M.Y., Phelan, J.P. *Obstetrics and Gynecology* 1985; **66:** 337.

Labor and delivery in the presence of mitral stenosis: central hemodynamic observations. Clark, S.L., Phelan, J.P. *et al. American Journal of Obstetrics and Gynecology* 1985; **152:** 984.

Cardiovascular alterations in severe pregnancy-induced hypertension seen with an intravenously given hydralazine bolus. Cotton, D.B., Gonik, B., Dorman, K.F. *Surgery Gynecology and Obstetrics* 1985; **161:** 240.

Glucocorticoids and beta-adrenergic-receptor agonists: their combined effect on fetal rabbit lung surfactant. Ekelund, L., Enhorning, G. *American Journal of Obstetrics and Gynecology* 1985; **152:** 1063.

Diabetes insipidus in pregnancy. Feldberg, D., Dicker, D. *et al. Israel Journal of Medical Sciences* 1985; **21:** 695.

The effect of oral ritodrine therapy on glucose tolerance in pregnancy. Main, D.M., Main, E.K. *et al. American Journal of Obstetrics and Gynecology* 1985; **152:** 1031.

A study of epidural fentanyl with and without epinephrine for post-Caesarean section analgesia. Robertson, K., Douglas, M.J., McMorland, G.H. *Canadian Anaesthetists' Society Journal* 1985; **32:** 502.

Effect of isoproterenol on uterine blood flow and cardiac output distribution in pregnant guinea pigs. Van De Walle, A.F.G.M., Martin, C.B. *American Journal of Obstetrics and Gynecology* 1985; **152:** 1058.

Epidural fentanyl in labour. An evaluation of the systemic contribution to analgesia. Vella, L.M., Willatts, D.G. *et al. Anaesthesia* 1985; **40:** 741.

Paediatric anaesthesia and intensive care

The management of cardiac arrest in infants and children. Bray, R.J. *British Journal of Hospital Medicine* 1985; **34:** 72.

Differential response of respiratory muscles to airway occlusion in infants. Carol, W.A., Miller, M.J., Martin, R.J. *Journal of Applied Physiology* 1985; **59:** 847.

Effects of positive end expiratory pressure during ventilation of the preterm infant. Field, D., Milner, A.D., Hopkin, I.E. *Archives of Diseases in Childhood* 1985; **60:** 843.

Neonatal effects of maternal nadolol therapy. Fox, R.E., Marx, C., Stark, A.R. *American Journal of Obstetrics and Gynecology* 1985; **152:** 1045.

Preferential blood flow increase to the brain stem in moderate neonatal hypoxia—reversal by naloxone. Lou, H.C., Tweed, W.A., Davies, J.M. *European Journal of Pediatrics* 1985; **144:** 225.

Airway protective and abdominal expulsive mechanisms in infantile regurgitation. Menon, A.P., Schefft, G.L., Thach, B.T. *Journal of Applied Physiology* 1985; **59:** 716.

Oral breathing in newborn infants. Miller, M.J., Martin, R.J. *et al. Journal of Pediatrics* 1985; **107:** 465.

Life-threatening complications of sickle cell disease in children. Mills, M.L. *Journal of the American Medical Association* 1985; **254:** 1487.

Trials of high frequency jet ventilation in preterm infants with severe respiratory disease. Pagani, G., Rezzonico, R., Marini, A. *Acta Paediatrica Scandinavica* 1985; **74:** 681.

Episodes of apnea and bradycardia in the preterm newborn—impact on cerebral circulation. Perlman, J.M., Volpe, J.J. *Pediatrics* 1985; **76:** 333.

Treatment of fetal cardiac arrythmias. Wladimiroff, J.W., Stewart, P.A. *British Journal of Hospital Medicine* 1985; **34:** 134.

Cardiovascular system

Physiology

Ionic movements and irreversible anoxic damage. Altschuld, R.A., Wenger, W.C., Brierley, G.P. *Basic Research in Cardiology* 1985; **80:** 151.

Regulation of blood coagulation and thrombosis. Briet, E., Engesser, L., Brommer, E.J.P. *Haemostasis* 1985; **157:** 228.

Hypokalemia from beta 2-receptor stimulation by circulating epinephrine. Brown, M.J. *American Journal of Cardiology* 1985; **56:** 3D.

Hepatic plasma flow during sodium nitroprusside-induced hypotension in humans. Chauvin, M., Bonnet, F. *et al. Anesthesiology* 1985; **63:** 287.

Peripheral circulation in hypertensive patients—findings by digital pulse plethysmography. Ferrara, L.A., Strazzullo, P. *et al. Artery* 1985; **12:** 346.

The role of the atria in fluid volume control. Kaye, G., Camm, A.J. *British Journal of Hospital Medicine* 1985; **34:** 82.

Effects of noradrenaline and isoproterenol on cardiopulmonary function in a canine model of acute pulmonary hypertension. Molloy, D.W., Lee, K.Y. *et al. Chest* 1985; **88:** 432.

Malignant arrhythmia in relation to serum potassium in acute myocardial infarction. Nordrehaug, J.E. *American Journal of Cardiology* 1985; **56:** 20D.

Mitral valve prolapse. Oakley, C.M. *Quarterly Journal of Medicine* 1985; **56:** 317.

Mechanisms of ischemic injury in the heart. SCHRADER, J. *Basic Research in Cardiology* 1985; **80:** 135.

Central nervous system mechanisms in blood pressure control. STRUTHERS, A.D., DOLLERY, C.T. *European Journal of Clinical Pharmacology* 1985; **28:** 1.

Prevention of epinephrine-induced hypokalemia by nonselective beta blockers. VINCENT, H.H., MAN, A.J. *et al. American Journal of Cardiology* 1985; **56:** 10D.

Treatment and medication

Drug treatment of heart failure. DOLLERY, C.T., CORR, L. *British Heart Journal* 1985; **54:** 234.

Effects of long-term therapy with labetalol on lipoprotein in patients with mild hypertension. HYLANDER, B., ELIASSON, K. *et al. Acta Medica Scandinavica* 1985; **218:** 51.

Effects of dopamine and dobutamine on hemodynamics and plasma catecholamine levels during severe lactic acid acidosis. KOSUGI, I., TAJIMI, K. *Circulatory Shock* 1985; **17:** 95.

Pacemaker Therapy. KOWEY, P.R., MULLAN, D.F., WETSTEIN, L. *Surgical Clinics of North America* 1985; **65:** 595.

Ventilatory effects of long-term treatment with pindolol and metoprolol in hypertensive patients with chronic obstructive lung disease. LAMMERS, J.W.J., FOLGERING, H.T.M. *et al. British Journal of Clinical Endocrinology* 1985; **20:** 205.

Progress in the surgical treatment of cardiac arrhythmias. LAWRIE, G.M., WYNDHAM, C.R.C. *et al. Journal of the American Medical Association* 1985; **254:** 1464.

Recent advances in cardiopulmonary bypass and the clinical application of myocardial protection. LAZAR, H.L., ROBERTS, A.J. *Surgical Clinics of North America* 1985; **65:** 455.

Antibiotic cover for cardiac surgery. Leading article *Lancet* 1985; **2:** 701.

Dextran and a modulator of immune and coagulation activities in trauma patients. MILLER, C.L., LIM, R.C. *Journal of Surgical Research* 1985; **39:** 183.

Corticosteroid agents in intensive care. OH, T.E. *Medical Journal of Australia* 1985; **143:** 290.

Effect of diuretic therapy on ventricular arrhythmias in hypertensive patients with or without left ventricular hypertrophy. PAPADEMETRIOU, V., PRICE, M. *et al. American Heart Journal* 1985; **110:** 595.

The pharmacodynamics and pharmacokinetics of a new calcium antagonist nisoldipine in normotensive and hypertensive subjects. PASANISI, F., MEREDITH, P.A., REID, J.L. *European Journal of Clinical Pharmacology* 1985; **29:** 21.

Digoxin interactions—the influence of quinidine and verapamil on the pharmacokinetics and receptor binding of digitalis glycosides. PEDERSEN, K.E. *Acta Medica Scandinavica* 1985; **218** (Suppl 697): 7.

Antiarrhythmic drug therapy (part 1). PODRID, P.J. *Chest* 1985; **88:** 452.

Slow channel calcium activators, a new group of pharmacological agents. Minireview. PREUSS, K.C., GROSS, G.J. *et al. Life Sciences* 1985; **37:** 1271.

Effects of continuous infusion of intravenous nitroglycerin on methemoglobin levels. SAXON, S.A., SILVERMAN, M.E. *American Journal of Cardiology* 1985; **56:** 461.

Respiration

Physiology

Ventilatory response to carbon dioxide and to isometric muscle contraction after administration of placebo, propranolol, mepindolol and salbutamol. BOSISIO, E., COLOMBO, F. *et al. Respiration* 1985; **48:** 116.

Measurement of tidal breath by determination of chest wall volume displacement in patients with airflow obstruction. DADZIE, C., SIMPSER, M., LAVIETES, M.H. *Chest* 1985; **88:** 420.

Lung fluid and protein flux during postoperative sepsis. HOLMAN, J.M., SABA, T.M. *et al. Circulatory Shock* 1985; **17:** 121.

Pulmonary function and electromyographic study of respiratory muscles in myotonic distrophy. JAMMES, Y., POUGET, J. *et al. Muscle and Nerve* 1985; **8:** 586.

Respiratory gas exchange in the assessment of patients with impaired ventricular function. LIPKIN, D.P., PERRINS, J., POOLE-WILSON, P.A. *British Heart Journal* 1985; **54:** 321.

Effect of respiratory apparatus on timing and depth of breathing in man. MAXWELL, D.L., COVER, D., HUGHES, J.M.B. *Respiration Physiology* 1985; **61:** 255.

Intraairway thermal profiles during exercise and hyperventilation in normal man. MCFADDEN, E.R., PICHURKO, B.M. *Journal of Clinical Investigation* 1985; **76:** 1007.

Pulmonary extraction of serotonin and propranolol in patients with adult respiratory distress syndrome. MOREL, D.R., DARGENT, F. *et al. American Review of Respiratory Disease* 1985; **132:** 479.

Cardiopulmonary response to inspiratory pressure support during spontaneous ventilation vs conventional ventilation. PRKASH, O., MEIJ, S. *Chest* 1985; **88:** 403.

Acute upper airway obstruction in the postburn period. WAYMARK, J.P., LAW, E. *et al. Archives of Surgery* 1985; **120:** 1042.

Treatment and medication

Obstructive sleep apnea: variations in surgical management. CALDARELLI, D.D., CARTWRIGHT, R.D. *et al. Laryngoscope* 1985; **95:** 1070.

Adult respiratory distress syndrome—prognosis after onset. Fowler, A.A., Hamman, R.F. *et al. American Review of Respiratory Disease* 1985; **132:** 472.

Central nervous system

Physiology

Blood-brain barrier and peptides. Ermisch, A., Ruhle, H.J. *et al. Journal of Cerebral Blood Flow and Metabolism* 1985; **5:** 350.

Normal average value of cerebral blood flow in younger adults is 50 ml/100 g/min. Lassen, N.A. *Journal of Cerebral Blood Flow and Metabolism* 1985; **5:** 347.

Sleep-wake complaints in patients with sleep-related respiratory disturbances. Roehrs, T., Conway, W. *et al. American Review of Respiratory Disease* 1985; **132:** 520.

Treatment and medication

Hepatic encephalopathy. Fraser, C.L., Arieff, A.I. *New England Journal of Medicine* 1985; **313:** 865.

The neuroleptic malignant syndrome—a review. Gibb, W.R.G., Lees, A.J. *Quarterly Journal of Medicine* 1985; **56:** 421.

Reversal of neurological deficits by levallorphan in patients with acute ischemic stroke. Handa, N., Matsumoto, M. *et al. Journal of Cerebral Blood Flow and Metabolism* 1985; **5:** 469.

Endocrine and metabolic

Physiology

Opioid peptides in human adrenal: partial characterization and presence of adrenal peptide E. Boarder, M.R., McArdle, W. *Journal of Clinical Endocrinology and Metabolism* 1985; **61:** 658.

Hemorrhagic shock and the central vasopressin and opioid peptide system of rats. Feuerstein, G., Molineaux, C.J. *et al. American Journal of Physiology* 1985; **249:** E244.

Effects of physiological concentrations of vasopressin on haemostatic function in man. Grant, P.J., Davies, J.A. *et al. Clinical Science* 1985; **69:** 471.

Value of glucose control in preventing complications of diabetes. Kilo, C. *American Medical Journal* 1985; **79:** 33.

Sodium balance in renal failure—a comparison of patients with normal subjects under extremes of sodium intake. Koomans, H.A., Roos, J.C. *et al. Hypertension* 1985; **7:** 714.

Effect of pentobarbital and hemorrhage on renal autoregulation. Kremser, P.C., Gewertz, B.L. *American Journal of Physiology* 1985; **249:** F356.

The stimulus for vasopressin release during laparoscopy. Melville, R.J., Frizis, H.I. *et al. Surgery Gynecology and Obstetrics* 1985; **161:** 253.

The role of plasma osmolality, angiotensin II and dopamine in vasopressin release in man. Morton, J.J., Connell, J.M.C. *et al. Clinical Endocrinology* 1985; **23:** 129.

Islet-cell abnormalities in non-insulin-dependent diabetes mellitus. Raskin, P. *American Journal of Medicine* 1985; **79:** 2.

Kidney function and drug action. Reidenberg, M.M. *New England Journal of Medicine* 1985; **313:** 816.

Glucagon physiology and pathophysiology in the light of new advances. Unger, R.H. *Diabetologia* 1985; **28:** 574.

Regulation of plasma vasopressin in insulin-dependent diabetes mellitus. Zerbe, R.L., Vinicor, F., Robertson, G.L. *American Journal of Physiology* 1985; **249:** E317.

Treatment and medication

Implantable infusion pump management of insulin resistant diabetes mellitus. Buchwald, H., Chute, E.P. *et al. Annals of Surgery* 1985; **202:** 278.

Effects of furosemide and captopril on submaxillary gland blood flow and arterial pressure. Catanzaro, O.L., Vila, S.B., Seeber, A.M. *Pharmacological Research Communications* 1985; **17:** 725.

Brittle diabetes—present concepts. Gill, G.V., Walford, S., Alberti, K.G.M.M. *Diabetologia* 1985; **28:** 579.

Metformin improved insulin resistance in type 1 insulin-dependent diabetic patients. Gin, H., Messerschmitt, C. *et al. Metabolism* 1985; **34:** 923

Enhancement of adrenal cortisol secretion after intravenous high dose dexamethasone. Graybeal, M.L., Fang, V.S., Landau, R.L. *Journal of Clinical Endocrinology and Metabolism* 1985; **61:** 607.

Furosemide ototoxicity: clinical and experimental aspects. Rybak, L.P. *Laryngoscope* 1985; **95:** 1 (Suppl).

The end of the crystalloid era? A new approach to perioperative fluid administration. Twigley, A.J., Hillman, K.M. *Anaesthesia* 1985; **40:** 860.

The metabolic response to the euglycemic insulin clamp in type 1 diabetes and normal humans. Zuniga-Guajardo, S., Zinman, B. *Metabolism* 1985; **34:** 926.

Pain

Treatment and medication

Inhibition of postoperative pain by continuous low-dose intravenous infusion of lidocaine. Cassuto, J., Wallin, G. *et al. Anesthesia and Analgesia* 1985; **64:** 971.

Ommaya reservoirs in 387 cancer patients—a 15 year experience. Obbens, E.A.M., Leavens, M.E. *et al. Neurology* 1985; **35:** 1274.

Intrathecal administration of beta-endorphine and dynorphin-(1-13) for the treatment of intractable pain. Wen, H.L., Mehal, Z.D. *et al. Life Sciences* 1985; **37:** 1213.

Other

Physiology

Maximal perfusion of skeletal muscle in man. ANDERSEN, P., SALTIN, B. *Journal of Physiology* 185; **366:** 233.

Treatment and medication

Comparison of antacid, sucralfate, cimetidine and ranitidine in protection of the gastric mucosa. TARNAWSKI, A., HOLLANDER, D. *et al. American Journal of Medicine* 1985; **79:** 19.

Anaesthesia, 1986, Volume 41, pages 454–463

News and notices

Stop Press. *Readers of this section are also referred to the Stop Press page at the end of this section.*

Obituaries

Adams, Adam Stanislaw, FFARCS, DA. Formerly consultant anaesthetist to the Llanelli group of hospitals. Qualified from Edinburgh University in 1949.

Bourne, Susan Patricia, FFARCS. Consultant anaesthetist at North Middlesex Hospital and St. Ann's Hospital, London. Qualified at Westminster Hospital Medical School in 1970.

Clayton, Richard Barnett, FFARCS, DA. Formerly consultant anaesthetist to Aylesbury Health District. Qualified at St. Bartholomew's Hospital in 1940.

Cuddigan, John Patrick, MB, BCH, BAO, DA. Formerly consultant anaesthetist to the Windsor group of Hospitals and Holloway Sanatorium. Qualified at the National University of Ireland in 1921.

Griffith, Harold Randall, Hon. FFARCS. Late Professor of Anaesthetics at Montreal, Canada and first President of the WFSA.

Hoggins, Eileen Mary, FFARCS, DA. Consultant anaesthetist Walsall group of hospitals. Qualified from the University of Birmingham in 1943.

Parke, Frederick William, MBE, DA. Late consultant anaesthetist South Worcestershire Hospital Group. Qualified from University of Dublin in 1938.

Ryder, David Alan, DA. Formerly anaesthetic registrar at Adelaide Hospital, Dublin. Qualified from University of Dublin in 1954.

Association of Anaesthetists of Great Britain and Ireland

The Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA, England. Telephone: 01–631 1650 (Ansafone service available out of office hours).

Standing notices

Full details of the activities of the Association are published in the January edition of *Anaesthesia* (106–111). These include details of membership, grants, (both travel and research) fees in independent practice, publications of the Association, educational and historical information.

Membership of Council

Group Captain C.A.B. Maclaren has replaced Colonel J. McEwan as the (coopted) representative of the Armed Forces.

Future Meetings of the Association

Annual Scientific Meetings

1986—London, 18–19 September.
1987—Sheffield, 10–11 September.
1988—Southampton, 15–16 September.

Linkman Conferences

1986—London, 17 September.
1987—Sheffield, 9 September.
1988—Southampton, 14 September.

Annual Scientific Meeting—London, 18–19 September 1986

A Free Paper session will be held during the Annual Scientific Meeting and facilities will be available for poster demonstrations. The closing date for applications for demonstration space and the free paper presentation is 30 June 1986. The title of poster demonstrations, the display area required, and summaries of free papers should be submitted to the Association office.

Competence to practise

The Association of Anaesthetists of Great Britain and Ireland and the Royal College of Psychiatrists are cooperating in a scheme to help sick anaesthetists early in their illness.

The system depends upon voluntary reporting by colleagues and is not coercive. It must be emphasised that this scheme is supplementary to existing controls. Fitness to practise may be impaired through illness and the sick doctor for various reasons may not take any steps to remedy the situation. The scheme provides machinery whereby confidential psychiatric help can be offered to the ailing doctor from a source outside his own Region.

The reporting clinician should contact the office of the Association of Anaesthetists to ascertain the name of a referee (Dr P.J. Helliwell, Dr D.C. Howat, Dr S.A. Mason) and need not identify himself to the office staff. The reporting clinician will be given the name, telephone number and availability of the referee. Preferably, a second clinician will also be required to confirm the report to the referee. The referee will then contact a psychiatrist from another Region nominated by the College of Psychiatrists from a prepared list: the psychiatrist will then get in touch with the potential patient.

No further information will be transmitted through the system unless the potential patient does not accept the offer of a visit to the nominated psychiatrist. In that case, the reporting physician(s) will be informed after a month that treatment has not been accepted.

Suitable arrangements have been made for confidential treatment of the doctor–patient in another Region and for the reimbursement of travel expenses.

Anaesthesia in the Developing World

The Association of Anaesthetists, through its International Relations Committee, receives many requests to provide lecturers and clinical instructors for Departments of Anaesthesia throughout the developing world.

There is considerable variety in the requirements of different locations, but the general policy of the Association is to provide an educational rather than a purely service commitment. Vacancies currently exist in Nigeria, Ghana, Zimbabwe and Zambia and are mostly of one year's duration (although occasionally shorter periods are required).

Anyone interested in service in a developing country who has the FFARCS diploma should write to Chairman of the International Relations Committee, Dr R.J. Eltringham, Department of Anaesthesia, Gloucestershire Royal Hospital, Gloucester GL1 3NN.

Recent publications of the Association of Anaesthetists of Great Britain and Ireland

Fees for anaesthetists in private practice. January 1986. *Post-anaesthetic recovery facilities.* 1985. *Professional references in the National Health Service.* Guidance and proforma, 1985. These, and earlier publications, are available from the Association office.

The Junior Anaesthetists' Group of the Association of Anaesthetists of Great Britain and Ireland

All junior members of the Association are members of the Group. The Group committee has representation on various committees of the Association and Faculty.

Committee

Chairman: Dr G.W. Hamlin (*1 Grange Park Close, Leeds, LS8 3BU. Tel. 0532 659114.* Council of the Association. JCHTA Manpower and Working Party of Faculty, Advisory Panel and Faculty Tutors).

Honorary Secretary: Dr Laurie Allan (*Pentland Grove House, Seafield by Roslin, Midlothian, Edinburgh EH25 9RQ. Tel. (031) 445 2313.* Hospital Junior Staff Committee, Council of Royal Society of Medicine, Editorial Board.).

Committee members: Dr A.D.J. Nicoll (*2 Hardwick Close, Ipswich IP4 5XB. Tel. (0473) 718432.* Faculty Education Committee, Safety Committee, Linkman Coordinator). Dr I. Woods (*40 Coppice Avenue, Sale, Cheshire, M33 4WB. Tel. (061) 962 8860.* International Relations Committee). Dr Nancy Redfern (*Westfield House, Acomb, Hexham, Northumberland. Tel. (0434) 607444.* Specialist Societies Committee). Dr Deborah Shiller (*4 Lisa Court, Downsland Road, Basingstoke, Hants. Tel. (0256) 477885.* CCHMS, Association Working Party on Manpower). Dr Anne Blyth (*7 Cleveden Gardens, Glasgow G12 0PU. Tel. (041) 34 9974*). Dr K.C. Lowry (*10 Sandhill Park, Co. Armagh, BT66 7AX Tel. (07622) 22628.* Coopted for Northern Ireland Meeting).

Representative of Council: Dr R.J. Eltringham (*Gloucester*).

Junior Group News

The committee would like to express their thanks to Dr T.B. Boulton who has resigned as representative from Council on the committee. His committee work on behalf of the juniors has been much appreciated. The committee would also like to thank Dr Wendy Scott who resigned as chairman after two years' service, on appointment to a consultant post. The two vacancies on the committee will be filled by ballot at the Cardiff meeting.

Annual Meeting

1987—Belfast, 8–10 April (Junior Linkman Meeting, April 7).

Faculty of Anaesthetists of the Royal College of Surgeons of England

The Faculty of Anaesthetists of the Royal College of Surgeons of England, 35–43 Lincoln's Inn Fields, London WC2A 3PN. Telephone: 01–405 3474

Faculty News

Frederic Hewitt Lecturer

Dr D.B. Scott has been appointed Frederic Hewitt Lecturer for 1987.

Fellowship ad eundem

Dr A.M.S. Black, FFARCS, has been elected to the Fellowship *ad eundem.*

Regional Educational Adviser

Dr J. Baldasera has been appointed Faculty Regional Eductional Advisor in the Northern region in succession to Dr L.J. Dunkin.

Nuffield Prize

The Nuffield Prize has been awarded to Dr S.S. Kee on the results of the Part 2 FFARCS examination held in October 1985.

Examination results

At the Part 1 FFARCS examination held in December 1985 171 of the 366 candidates were successful.

Postgraduate accommodation

Bernard Johnson House, Fortis Green, London N2 9EX is a Foundation supported by private endowment by the British Council to maintain furnished flats for the use of full time postgraduate students who are married with no more than two children. Leases are for six months to eighteen months only. The flats are available to all members of surgical and medical faculties and the endowment gives priority to anaesthetists. British and overseas students are eligible. For further information write to the Warden at the above address.

Faculty of Anaesthetists of the Royal College of Surgeons in Ireland

The Faculty of Anaesthetists of the Royal College of Surgeons in Ireland, 123 St Stephen's Green, Dublin 2. Telephone: Dublin 780200 (Ext 268).

Dean: Dr P.W. Keane.
Vice-Dean: Dr D.C. Moriarty.
Honorary Secretary: Dr D.F. Hogan.
Honorary Treasurer: Dr J.C. Cooper.

Annual Scientific Meeting, 1986

This meeting will be held on May 16–17 1986. There will be three topics: Adverse drug reactions, Anaesthetic applications of computers, and Muscle relaxants. The speakers include, Prof. J.B. Forrest (*Canada*); Dr S. McCann (*Dublin*); Prof. D. Campbell (*Scotland*); Dr G. Kenny (*Scotland*); Dr M. Slazenger (*Dublin*); Dr W.S. Wren (*Dublin*); Dr A. Synnott (*Dublin*); Dr W.C. Bowman (*Scotland*); Dr R.K. Mirakhur (*Belfast*).

The *Gilmartin Lecture* will be delivered by Professor Sir J. Gordon Robson, CBE, DSc, FRCS, FFARCS, FFARCSI (Hon) on May 16.

Faculty Lectures, 1986

Autumn, September 26.
Winter, December 12.

FFARCSI Examinations, 1986

Part 1, October 17 (closing date, September 5); part 2, October 24 (closing date, September 12); part 3, November 28 (closing date, October 17). *Revision course* (Part 2) October 8–15.

For further information please write to the Honorary Secretary, Faculty of Anaesthetists, Royal College of Surgeons in Ireland, Dublin 2.

Section of Anaesthetics of the Royal Society of Medicine

Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE. Telephone: 01–580 2070

President: Dr Aileen K. Adams.
Secretaries: Dr I.M. Verner (*Department of Anaesthetics, The Middlesex Hospital, Mortimer Street, London W1N 8AA*), Dr G.M.C. Patterson (*Oxford*).

Meetings of the Section are held on the first Friday in the month and are held at 1 Wimpole Street, London W1M 8AE, at 5.30 p.m.

Fellows of the RSM are welcome to bring guests if they wish.

Programme

1986

18 April—*Hepatotoxicity of halothane—an enigma of drug toxicity.* Professor M.J. Cousins (*Australia*).
9 May—*May & Baker R.S.M. Prizes Essays. Annual General Meeting. Annual Dinner.*
6 June—*All-day symposium: Anaesthesia and ENT surgery.*

Specialist Societies

British Association for Immediate Care (BASIC)

Chairman: K.C. Easton, OBE.
Secretary: Hamish McLeod (*The Hope, Moffat Dumfriesshire. Tel: Moffat 20314*).

Society of Anaesthetists of the British Forces in Germany

President: Professor J.P. Payne (London).
Secretary: Major S.T. Inglis, FFARCS, RAMC (BMH Rinteln, BFPO 20 Germany).

Association of Cardiothoracic Anaesthetists

Honorary Secretary: Dr R.D. Latimer (*Papworth Hospital, Papworth Everard, Cambridge CB3 8RE. Tel: 0480 830541*).

Future meetings

1986—Inaugural Meeting of the European Association of Cardiovascular Anaesthetists.
17–18 June, Cambridge.
Information: Dr R.D. Latimer.
2–5 September, Munich.
Anaesthesia for cardiac patients.
Information: ISACP/Interplan (*Sophienstrasse 1, 8000 Munchen 2*).
12 December, London.
Information: Dr R. Feneck (*London Chest Hospital, Bonner Road, London E2 9JX*).
1987—Spring Meeting—Cambridge.
Information: Dr I. Hardy (*Papworth Hospital, Papworth Everard, Cambridge CB3 8RE*).
Autumn Meeting—Liverpool.
Information: Dr J.C. Richardson (*Broadgreen Hospital, Thomas Drive, Liverpool L14 3LB*).

Association of Dental Anaesthetists

President: Dr T.M. Young (*Manchester*).
Secretary: Dr M.A. Skivington (*Department of Anaesthetics, Poole General Hospital, Poole, Dorset BH15 2JB*).
Assistant Secretary/Editor: Dr M.E. Ward (*Oxford*).

Future Meetings

1986—27–28 June. Manchester Royal Infirmary.
Information: Dr T.M. Young (*Department of Anaesthetics, Royal Infirmary, Manchester M13*).
1987—17 January. Queen Elizabeth Hospital, Postgraduate Medical Centre, Birmingham.
Information: Dr P.J. Tomlin.
11 July. Plymouth.
Information: Dr F.S. Keddie.

Intensive Care Society

Chairman: Dr Sheila M. Willatts (*Bristol*).
Meetings Secretary: Dr C.J. Hinds (*St Bartholomew's Hospital*).
Secretary/Treasurer: Dr D. Ryan (*Intensive Therapy Unit, Freeman Hospital, Newcastle upon Tyne NE7 7BE*).

Future meetings

1986—11–12 April. Newcastle upon Tyne.
1 November, Hospital for Sick Children, London.
1987—9–11 April. Exeter University.

The Intractable Pain Society of Great Britain and Ireland

Chairman: Dr H. Rafferty (*Dublin*).
Vice-Chairman/Chairman Elect: Dr K. Budd (*Bradford*).
Honorary Secretary: Dr T.P. Nash (*Basingstoke District Hospital, Aldermaston Road, Basingstoke, Hampshire RG24 9NA*).

Prize Essay

An annual competition is held for the best essays related to pain relief. Submissions to the Honorary Secretary by 31 August 1986. Essay contests are judged in two groups. Doctors in training and Society members.

Future meetings

1986—3–5 April—Back Pain Association, Norwich.
12–16 May—Hospice Care Conference, Lee Abbey, Lynton, North Devon.
17–20 June—Scottish Terminal Care Meeting, St Andrews.
26–29 June—Annual General Meeting and Scientific Meeting, Belfast.
Hosts: Drs W.B. Loan, R. Armstrong and J. Cooper.
26 September—Joint Meeting of the British Medical Acupuncture Society, Royal Society of Medicine.
1987—Annual General Meeting and Scientific Meeting, Liverpool.
Hosts: Drs C. Wells and S. Lipton.

Neuroanaesthetists' Travelling Club

Information: Dr S.B. Foulds, Salford Health Authority, Peel House, Albert Street, Eccles, Manchester M30 0NJ.

Obstetric Anaesthetists' Association

President: Dr D.D. Moir (*Glasgow*).
Honorary Secretary: Dr J. Thorburn (*Department of Anaesthesia, The Queen Mother's Hospital, Yorkhill, Glasgow G3 8SH*).
Treasurer: Dr A.P. Rubin (*London*).
Minute Secretary: Dr B.R. Wilkey (*Cambridge*).
All UK membership enquiries to Dr J. Thorburn, please.

Award

The Association's Gold Medal has been awarded to Professor M. Rosen (*Cardiff*).

Future meetings

1986—21 March. Dundee, Scotland.
Host: Dr R. Milne.
4–5 September, Coleraine, N. Ireland.
Host: Dr J. Moore.
Information about meetings is available from the host.

Association of Paediatric Anaesthetists

President: Dr G.W. Black (*Belfast*).
Honorary Secretary: Dr P. Morris (*Royal Manchester Children's Hospital, Pendlebury, Manchester M27 1HA*).

Future meetings

1986—28 May–4 June. Joint meeting with the Swedish Society of Anaesthetists in Gothenburg and Stockholm.
Information: Dr W.R. Hain (*University Hospital, Queen's Medical Centre, Nottingham NG7 2YH*).
1987—20–21 March. Leeds.
Information: the Honorary Secretary.

Plastic Surgery and Burns Anaesthetists

President: Dr C.C.M. Howie (*Bangour*).
Honorary Secretary: Dr F.J.M. Walters (*Department of Anaesthetics, Frenchay Hospital, Bristol BS16 1LE*).
Enquiries about membership to the Honorary Secretary, please.

Future meeting

1986—27 September. Whiston, Merseyside.
Information Dr C.S. Ince (*Department of Anaesthetics, St Helen's Hospital, St Helen's, Merseyside WA9 3EA*).

The Russell Davies and Stuart Laird Prize

The Society wishes to announce that this prize, £200, has been generously donated by Abbott Ltd. The prize will be awarded for an essay connected with anaesthesia and plastic and burns surgery and is open to any career anaesthetist in the National Health Service. Applications are invited for the prize which is to be awarded in October 1986. Further details are obtainable from the Honorary Secretary.

Anaesthetic Research Society

Chairman: Professor A.A. Spence.
Honorary Secretary: Dr A.R. Aitkenhead (*University Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW*).

Future meetings (closing dates for papers)

1986—11–12 April (28 February). University of Leeds.
4–5 July (May 23). University of Newcastle.
15 November (3 October). St Bartholomew's Hospital, London.

Special notice

Abstracts are photoreduced and must be submitted on a preprinted form, which is available from the Hon. Secretary. All correspondence and abstracts should be sent to the Hon. Secretary.

Resuscitation Council (UK)

Chairman: Mr A. Marsden.
Secretary: Dr D.A. Zideman (*Department of Anaesthetics, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS*).

Advanced life support

Posters which illustrate the Council's recommendations for Advanced Life support are now available.

Home news and notices

Honours

Dr M. Seigleman was appointed to the Order of the British Empire for Services to the East Lancashire Hospice.

Consultant appointments

Dr P.A. Acharya—King Khalid Eye Specialist Hospital, Riyadh, Saudi Arabia.
Dr S.J. Carter—Northern RHA.
Dr N.W.B. Clowes—North Staffordshire HA.
Dr N.H. Duncan—East Anglian RHA.
Dr M.A.P. Durkin—Gloucester Royal Infirmary, Bristol & Weston HA.
Dr A. Ferguson—Canterbury and Thanet HA.
Dr R.M. Foxell—Wessex RHA.
Dr S.L. Hill—Wessex RHA.
Dr P.C.W. Hunt—East Anglian RHA.
Dr J. Jenkins—Eastern General Hospital, Edinburgh.
Dr P.R. Layman—Trent RHA.
Dr S.S. Lowe—East Anglian RHA.
Dr S.W. Millar—South East Staffordshire and North Birmingham HA.
Dr A. Naunton—East Anglian RHA.
Dr D.C. Phillips—Trent RHA.
Dr P.D. Phillips—East Anglian RHA.
Dr V. Price—East Anglian RHA.
Dr S.N. Saggar—BMH Munster, Germany.
Dr S.A. Siddiqui—Calderdale Health Authority.
Dr P. Smith—Trent Regional HA.
Dr S.R. Swindells—St. James's University Hospital, Leeds.
Dr S. Taylor—Leicestershire HA.
Dr D.A.B. Turner—Leicestershire HA.

National and local events

The diary is collated by Dr A. Padfield, Consultant Anaesthetist, Royal Hallamshire Hospital, Sheffield S10 2RX. Society secretaries are invited to submit their programmes to him.

April 1986

7–25 *Faculty, London.* Course on Anaesthetics for Part 3 FFARCS.
Information: Courses Assistant, Faculty of Anaesthetists, 35/43 Lincoln's Inn Fields, London WC2A 3PN.

8–10 *Junior Anaesthetists Group.* AGM and Annual Scientific Meeting at Cardiff.
Information: Association of Anaesthetists, Rooms 475, Tavistock House South, Tavistock Square, London WC1H 9LG.

8–9 *West Midlands Intensive Care Group.* 6th Annual Meeting at Wyddrington Hall.
Guest Speaker: Dr Margaret Branthwaite.
Information: Miss M.C. Wood, PGMC, East Birmingham Hospital, Birmingham B9 5ST.

8–9 *Blood Flow Group, Biological Engineering Society:* Obstetric and Neonatal Blood Flow.
Information: Biological Engineering Society Royal College of Surgeons, 35/43 Lincoln's Inn Fields, London, WC2A 3PN.

9 *Northern Ireland Society.* AGM and Dr D.L. Coppel: *High frequency ventilation (film).*
Information: Dr J.E. Hegarty, Department of Anaesthetics, 97, Lisburn Road, Belfast BT9 7BL.

9 *Reading Anaesthetists.* Dr M. Cowen, *The problems of running a D.G.H. Anaesthetic Service with Reduced Junior Staff.*
Information: Dr A. Marshall Barr, Anaesthetics Department, Royal Berkshire Hospital, Reading RG1 5AN.

11 *One Day Symposium: Halothane and the liver: the problem revisited.*
Information: Anaesthetic Secretary, Bristol Royal Infirmary, Bristol BS2 8HW.

11–12 *Anaesthetic Research Society* at Leeds.
Information: Dr A.R. Aitkenhead, University Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW.

11–12 *Intensive Care Society.* Spring Meeting *at Newcastle upon Tyne.*
Information: Dr D.W. Ryan, Freeman Hospital, Newcastle upon Tyne NE7 7DN.

16 *FFARCS Pt 2 Papers,* London.

17 *FFARCS Pt 3* applications due, London.

17 *Section of Anaesthetics, Manchester Medical Society.* Out of Town Meeting, Lancaster Medical Centre, Lancaster Royal Infirmary. *Symposium on Pain Relief.*
Chairman: Mr P.D. Challen; Dr A. Kilpatrick: Acupuncture.
Host: Dr M.A. Rucklidge, Anaesthetics Department, Lancaster Royal Infirmary, LA1 4RP.
Information: Dr E.E.M. Thompson, University of Manchester, Oxford Road M13 9PL.

10 *Section of Anaesthetics, Royal Society of Medicine.* Prof. M.J. Cousins, Adelaide.
Hepatotoxicity of halothane: an enigma of drug toxicity.
Information: Sections Office, R.S.M. 1, Wimpole Street, London W1M 8AE.

19 *North of England Society.* Symposium: *Obstetric Anaesthesia and Analgesia.*
Information: Dr J.E. Charlton, Department of Anaesthesia, Royal Victoria Infirmary NE1 4LP.

19 *North East Thames Regional Society of Anaesthetists, Spring Meeting.*
Information: Dr E. Gibbs, Anaesthetic Department, Basildon Hospital, Basildon, Essex.

22 *Glasgow and West of Scotland Society of Anaesthetists.* AGM.
Information: Dr D.S. Arthur, Royal Hospital for Sick Children, Glasgow G3 8SJ.

25–27 *Scottish Society of Anaesthetists.* Annual Meeting at Peebles Hotel Hydro.
Information: Dr W.F.D. Hamilton, Ninewells Hospital, Dundee DD1 9SY.

28 *Wessex Anaesthetic Club.* Prof. W.S. Nimmo. *New directions in the administration of analgesics after surgery.*
Information: Dr D.V. Rutter, Department of Anaesthesia Southampton General Hospital.

May 1986

2 *Faculty Scientific Meeting:* Prediction and Control Drug Administration: *Bristol.*
Information: Faculty of Anaesthetists, 35/43 Lincoln's Inn Fields, London WC2A 3PN.

2 *FFA Part 1/DA(UK) applications due.*

6 *Edinburgh and East of Scotland Society of Anaesthetists:* AGM.
Information: Dr D.G. Littlewood, Anaesthetics Department, Royal Infirmary, Edinburgh EH3 9YW.

7 *Sheffield Anaesthetists* Dr J.F. Nunn. *Surgery in the Egyptian Old Kingdom.*
Information: Dr N.R. Bennett, Royal Hallamshire Hospital, Sheffield S10 2RX.

9 *Section of Anaesthetics, Royal Society of Medicine.* M and B Registrars Prizes.
AGM and Annual Dinner.
Information: Sections Office, RSM, 1, Wimpole Street, London W1M 8AE.

9 *Liverpool Society of Anaesthetists.* 54th AGM, Crewe Hall.
Information: Dr Anne M. Florence, Broadgreen Hospital, Liverpool L14 3LB.

9 *North of England Society of Anaesthetists.* Prof. A.P. Adams, *The fat man and the gas man.*
Information: Dr J.E. Charlton, Department of Anaesthesia, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP.

10 *Neuro-anaesthetists Travelling Club.* National Hospital for Nervous Diseases.
Information: Dr S. Ingram, The National Hospital, Queen Square, London WC1N 3BG.

12 *FFA Part 2* vivas start.

13 *Reading Anaesthetists.* Sq. Ldr R.M. Harding. *Aviation medicine*—the safe passage of an aircraft.
Information: Dr A. Marshall Barr, Anaesthetics Department, Royal Berkshire Hospital, Reading, Berks RG1 5AN.

15 *Section of Anaesthetics, Manchester Medical Society.* Prof D. Campbell, *Let your science be human—the Hunterian legacy.*

Information: Dr E.E.M. Thompson, University of Manchester, Oxford Road M13 9PL.

16–17 *Faculty of Anaesthetists, Ireland.* Annual Scientific Meeting. *Adverse Drug Reactions; Computers in Anaesthesia; Muscle Relaxants.*
Information: Dr D.F. Hogan, Faculty of Anaesthetists, St Stephen's Green, Dublin 2.

16–17 *Society of Anaesthetists of Wales.* Annual Summer Meeting, at Newport.
Information: Dr R. Mason, Department of Anaesthesia, Morriston Hospital, Swansea SA6 6NL.

22–24 *South West Society of Anaesthetists.* Meeting in Copenhagen.
Information: Dr J.A. Clement, Bristol Royal Infirmary, Bristol, BS2 8HW.

June 1986

4 *Sheffield Anaesthetists.* Dr Sheila Willatts, *Aspects of parenteral nutrition.*
Information: Dr G.P.M. Clark, Northern General Hospital, Sheffield S5 7AU.

6 *Section of Anaesthetics, Royal Society of Medicine.* All day Symposium. *Anaesthesia and E.N.T. surgery.*
Information: Sections Office, RSM, 1, Wimpole Street, London W1M 8AE.

6 *Scottish Society of Anaesthetists.* Registrars Meeting at Ninewells Hospital.
Information: Dr W.F.D. Hamilton, Ninewells Hospital, Dundee DD1 9SY.

7 *First Meeting* of the Society for the Study of the History of Anaesthesia, at *Royal Berkshire Hospital, Reading.*
Information: Dr T.B. Boulton, Royal Berkshire Hospital, Reading, Berks, RG1 5AN.

10 *Reading Anaesthetists.* Dr Jean Lumley: *Planning for failed intubation.*
Information: Dr A. Marshall Barr, Royal Berkshire Hospital, Reading, Berks RG1 5AN.

13 *FFA Part 1/DA (UK)* written papers begin.

14 *South East Thames* jointly with *Southern Society of Anaesthetists* at Eastbourne.
Information: Dr P.B. Hewitt, Department of Anaesthetics, Guy's Hospital, SE1 9RT.

17–18 *European Society of Cardiovascular Anaesthetists* at Cambridge.
Information: Dr R.D. Latimer, Papworth Hospital, Cambridge CB3 8RE.

23–27 *Faculty Course.* Current topics in anaesthesia.
Information: Courses Assistant, Faculty of Anaesthetists, 35/43, Lincoln's Inn Fields, London WC2A 3PN.

24–27 *Third European Congress of Obstetric Anaesthesia & Analgesia* at Trinity College, Dublin.
Information: Congress Secretariat, 44, Northumberland Road, Dublin 4, Ireland.

26–28 *Intractable Pain Society Meeting.* Belfast.
Host: Dr W.B. Loan, Whitla Medical Building, 97, Lisburn Road, Belfast BT9 7BL.

28 *Association of Dental Anaesthetists* at the Manchester Medical School.
Host: Dr T.M. Young, Department of Anaesthetics, Royal Infirmary, Manchester M13.

30 FFA Part 3 vivas begin.

July 1986

4–5 *Anaesthetic Research Society* at University of Newcastle.
Information: Dr A.R. Aitkenhead, University Department of Anaesthesia, Leicester Royal Infirmary, Leicester, LE1 5WW.

14 *FFA Part 1/D A (UK)* vivas begin.

International congress calendar

1986

15–18 April. Brussels. *Sixth International Symposium on Intensive Care and Emergency Medicine.*
Information: Dr J.L. Vincent, Department of Intensive Care, Erasmus University Hospital, Route de Lennik 808, 1070 Brussels (Belgium).

26 April. Ghent, Belgium. European Society of Regional Anaesthesia.
Information: Professor G. Rolly, Department of Anaesthesia, Academic Hospital, De Pintelaan 185, B-9000, Ghent, Belgium.

10–16 May. Adelaide, Australia. Faculty of Anaesthetists and the Royal Australasian College of Surgeons Annual General Scientific Meeting.
Information: Administrative Officer, Faculty of Anaesthetists, R.A.C.S., Spring Street, Melbourne, 3000, Victoria.

26–30 May. Washington, D.C. *Annual Meeting American Society of Critical Care Medicine.*
Information: SSCM, 223E, Imperial Way, Suite 110, Fullerton, CA 92635, USA.

28 May–3 June. Gothenburg and Stockholm. Association of Paediatric Anaesthetists and Swedish Society of Anaesthetists Joint Congress on *Paediatric Anaesthesia and Intensive Care.*
Information: Dr B. Ekstrom Jodal, Anestesiavdelning, Ostrajukhuset, Gothenburg, Sweden.

7–11 June. Scottsdale, Arizona. *Ninth Annual Conference on Shock.*

Information: Shock Society, Dr Sherwood M. Reichard, Medical College of Georgia, Augusta, Georgia 30912, USA.

11–14 June. Hamburg. *2rd European Congress on Intensive Care Medicine.*

Information: Hamburg Messe und Congress, GmbH, Postfach 30 24 80, D 2000, Hamburg 36, Federal Republic of Germany.

14–21 June. Cannes, France. *American & European Views on Critical Care.*

Information: N.W. B. Craythorne, Department of Anesthesiology, PO Box 016370, Miami, Florida, 33101, USA.

15–18 June. Graz, Austria. *Symposium on Computers in Critical Care and Pulmonary Medicine.*

Information: Dr G. Wiesspeiner, CCCPM, C/o Institute of Anaesthesiology, LKH Graz, Auenbruggerplatz 5, A-8036 Graz, Austria.

19–22 June. Barcelona, Spain. *8th Annual Meeting of European Academy of Anaesthesiology.*

Information: Prof. M.A. Nalda-Felipe, Department of Anesthesiology, Hospital Clinico, Facultad de Medicina, Villarroel 170, 08036 Barcelona, Spain.

24–27 June. Dublin. *Third European Congress of Obstetric Anaesthesia and Analgesia.*

Information: Congresses and Expositions Ltd, 44 Northumberland Road, Dublin 4, Ireland.

15 August. Msida, Malta. IV Annual Conference of the Association of Anaesthesiologists, Malta Medical School.

Information: The Secretary, PO Box 15, Msida, Malta.

20–23 August. Hamilton, New Zealand. *1986 Conference of Anaesthetists of New Zealand.*

Information: The Organising Committee, CANZ 86, Department of Anaesthesia, Waikato Hospital, Hamilton, New Zealand.

27–30 August. Rotterdam, The Netherlands. *First European Congress of Paediatric Anaesthesia.*

Information: Dr H.J. Manschot, Department of Anesthesiology, Sophia Children's Hospital, Gordelweg 160, 3038 GE Rotterdam, The Netherlands.

3–6 September. Malmo, Sweden. *Fifth Congress of the European Congress of Regional Anaesthesia.*

Information: Anestesikliniken, Malmo Allmanna Sjukhus, S 21401 Malmo, Sweden.

3–6 September. Rotterdam, The Netherlands. *Fourth International Symposium on Computing in Anaesthesia and Intensive Care.*

Information: Omar Prakash, MD, Thorax Centrum, PO Box 1738, 3000 DR Rotterdam, The Netherlands.

7–13 September. Vienna. *7th European Congress of Anaesthesiology.*

Information: Professor K. Steinbereithner, Spitalgasse 23, A-1090 Vienna, Austria.

16–19 September. Haifa, Israel. *14th International Congress of the Israel Society of Anesthesiologists.*

Information: Congress Secretary, PO Box 50006, Tel Aviv 61500, Israel.

18–19 September. London, England. *Annual Scientific Meeting of the Association of Anaesthetists of Great Britain and Ireland.*

Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9, Bedford Square, London, WC1 B3RA.

24–26 September. Leicester. *Royal College of Surgeons Annual Provincial Meeting (Anaesthetic Section).*

Information: Royal College of Surgeons of England, 35–43 Lincolns Inn Fields, London, WC2A 3PN.

18 October. London. *Postgraduate Study Day (Joint Meeting with the Faculty).*

Information: Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

20–22 November. Cleveland, Ohio. *Anesthesia and the Heart Patient.*

Information: Lisa Politi, Center for Continuing Medical Education, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, Ohio 44106, USA.

23–28 November. Florianopolis, Santa Catarina. *33rd Brazilian Congress of Anesthesiology.*

Information: Carlos A. Da Silva Junior, MD, Alameda Adolfo Konder 25, 88.000 Florianopolis, Santa Catarina, Brazil.

27–30 November. Grenoble, France. *4th International Conference on Disaster Medicine.*

Information: Ste Intern, Medecine de Catastrope, PO Box 59, CH 1213, Petit Lancy 2 France.

1987

7–9 May. Paris. *VI Annual Meeting of the European Society of Regional Anaesthesia.*

Information: M.A.P.A.R., Departement d'Anesthesiologie, Hopital de Bicetre, 94270 Kremlin-Bicetre, France.

16–22 May. Perth, Australia. Faculty of Anaesthetists and the Royal Australasian College of Surgeons Annual General Scientific Meeting.

Information: Administrative Assistant, Faculty of Anaesthetists, R.A.C.S., Spring Street, Melbourne, 3000 Victoria.

20–25 June. Montreal, Canada. XIII International Symposium on Cerebral Blood Flow and Metabolism.

Information: Sorelcomm (1985) Inc., Conference Secretariat, 1425 Dorchester Boulevard West, Montreal, Canada.

20–23 July. London. *2nd International Symposium of the History of Anaesthesia.*

Information: Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

23–25 July. Oxford, England. 50th anniversary of the

founding of the Nuffield Department of Anaesthetics.
Information: Nuffield Department of Anaesthetics, Department GP/87, Radcliffe Infirmary, Oxford OX2 6HE.

2–7 August. Hamburg, West Germany. *Vth World Congress on Pain.*
Information: 5th World Congress on Pain, c/o Hamburg Messe und Congress GmbH, Congress Organization, Postfach 30 24 80, 2000 Hamburg 36, West Germany.

10–11 September. Sheffield, England. *Annual Scientific Meeting of the Association of Anaesthetists of Great Britain and Ireland.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9, Bedford Square, London, WC1B 3RA.

1988

1–6 May. Brisbane, Australia. Faculty of Anaesthetists and the Royal Australasian College of Surgeons Annual General Scientific Meeting.
Information: Administrative Officer, Faculty of Anaesthetists, R.A.C.S., Spring Street, Melbourne, 3000 Victoria.

22–28 May. Washington, DC. *9th World Congress of Anaesthesiology.*
Information: American Soc. of Anaesthesiologists, 515 Busse Highway, Park Ridge, Illinois 60068, USA.

15–16 September. Southampton, England. *Annual Scientific Meeting of the Association of Anaesthetists of Great Britain and Ireland.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9, Bedford Square, London WC1B 3RA.

Anaesthesia, 1986, Volume 41, pages 464–468

The Annual Conference of Linkmen of the Association of Anaesthetists of Great Britain and Ireland, 1985

The Annual Conference of Linkmen was held in the Leicester Polytechnic on Wednesday 11 September 1985.

The President, Dr T.B. Boulton was in the chair throughout the meeting. He welcomed the 160 linkmen present and stressed the value placed by Council on the information and views received through the linkman organisation.

Association of Anaesthetists' appeal for nine Bedford Square

Dr M. Rosen, Vice-Chairman of the Appeal, outlined the progress which had been made with the Appeal since its launch in September 1984. Donations from anaesthetists now totalled around £120,000 towards a target for this group of £300,000 but he stressed that this had been achieved by donations from a very small proportion of the membership. Approaches to industry and to trusts were more likely to succeed if enthusiastic support from the membership was apparent. He reported that only 20% of linkmen had made donations and he encouraged those who had not already done so to visit the Association stand at the technical exhibition where donations would be accepted. At the same time and because of the limited duration of the Appeal, which is to close at the end of 1986, Dr Rosen asked for the renewed and enthusiastic support of linkmen in approaching anaesthetists throughout the country to persuade them to contribute. He again outlined the value of making donations by covenant which, because of the charitable status of the Association, allowed substantial amounts of tax to be reclaimed.

Dr Rosen reported that the house at Nine Bedford Square was now nearing the completion of its refurbishment and would provide the specialty with its own headquarters and home. This centre would not only contain the administrative offices of the Association, but would also create ideal accommodation for small seminars and discussion groups. Plans were already in hand for many such meetings. Space and secretarial assistance for some of the specialist anaesthetic societies were under discussion and there will be a library holding current and historical publications, a museum of historical equipment and a members' room for social gatherings. The President thanked Dr Rosen for his presentation.

National issues of the day

Dr M.M. Burrows, Honorary Treasurer, Chairman of the Central Committee for Hospital Medical Services detailed many matters under discussion which had implications for members of the profession in general and for anaesthetists in particular. He noted with regret the frequent failure by many bodies, including the Government, to consult with the profession on vital issues. The appointment of General Managers was likely to increase rather than reduce this problem. While it was accepted that changes in the Health Service were necessary, it was vitally important that these changes were brought about by management only after due consultation with the profession. He then highlighted several areas of particular concern. These included Nurse Education, where the proposed movement of nurse training to Colleges of Further Education would reduce the already often inadequate levels of cooperation between nursing and medical staff, the setting up of Management Boards in DGH's with District Managers largely drawn from the ranks of administrators, anxieties over private practice and the implications of a new document being prepared by the DHSS on this subject.

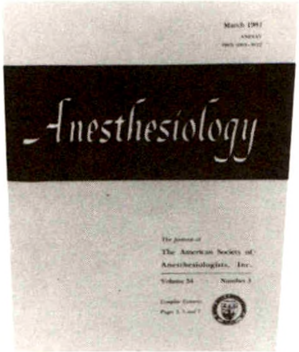
Discussion. Dr A.J. Whitaker (*Mansfield*) warned that private practice must not be allowed to conflict with NHS practice and he also supported a sympathetic attitude to the changing role of the nurse. Dr M. Rosen (*Cardiff*) expressed the view that the Association should actively encourage group private practice, thereby often reducing conflict between private and NHS work. Dr A. Padfield (*Sheffield*) drew attention to audits of theatre working practices being undertaken by administrators who might subsequently be unable to interpret the findings. He proposed that these studies should be undertaken by the profession and received considerable support for his views. Dr D.T. Protheroe (*Bath*) pointed out that shortages of anaesthetists were often blamed for cancellation of operating lists but that records kept in his Region had identified absences of surgeons to be the cause of a high proportion of cancellations.

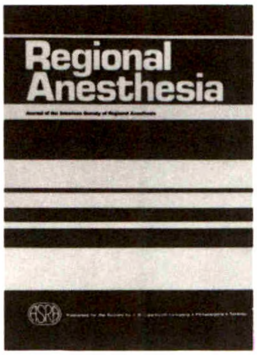
Confidential enquiry into perioperative deaths

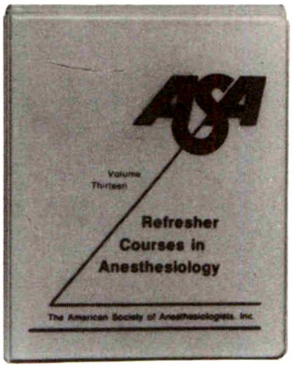
Dr J.N. Lunn (*Cardiff*) reported the present position of

Journals of Interest to ANESTHESIOLOGISTS

Indispensable tools for maintaining professional competency







ASA
Volume Thirteen
Refresher Courses in Anesthesiology
The American Society of Anesthesiologists, Inc.

ANESTHESIOLOGY

Journal of the American Society of Anesthesiologists, Inc.

Lawrence J. Saidman, M.D., Editor-in-Chief

Anesthesiologists nationwide look to this distinguished journal for current information on all facets of anesthesiology: pharmacologic bases of anesthesia; clinical principles, practices, and techniques; anesthesia management; complications of anesthesia and surgery; and more. The information is published in articles, reviews, current comments, editorial views, case reports, abstracts of current literature, and book reviews.

Published monthly. Individual rate $30.00 per year (U.S.), $65.00 (elsewhere).

REGIONAL ANESTHESIA

Journal of the American Society of Regional Anesthesia

Phillip O. Bridenbaugh, M.D., Editor

For the growing number of those concerned with the burgeoning specialty of regional and local anesthesia, this quarterly journal publishes highly informative articles on the clinical applications of current research and on professional issues and developments.

In addition to original articles, regular features include review articles discussing the current status of particular facets of the field; abstracts from other journals, especially international publications; case reports; clinical reports; correspondence; announcements of professional events; and editorials.

Highlights each year include the full text of the Labat Address, focusing on the humane and philosophical foundations of this field; and the Abbott Lecture, a scholarly and lively look at a particular aspect of regional and local anesthesia and its present implications.

Published quarterly. Individual rate $35.00 (U.S.), $40.00 (elsewhere). Residents $23.00 (U.S. only.)

ASA Refresher Courses in Anesthesiology

A Project in the Continuing Education Program of the American Society of Anesthesiologists

Paul Barash, M.D., Editor

Each annual volume in this popular series consists of thirteen to seventeen complete and edited lectures selected from regional and national ASA Refresher Courses. Individually bound, the lecture ''chapters'' are printed as separate booklets and gathered into an attractively designed looseleaf binder. This format contributes to an orderly file of information for use as a working reference and a continuously updated additon to your personal library. It allows you to tailor it to your own ideas and needs by refiling, reclassifying, or supplementing the material with your own notes, reprints or other material.

Published annually. Individual rate (per volume) $15.00 per year (U.S.). $20.00 (elsewhere). Thirteen volumes are currently available.

1792

J. B. Lippincott Company • *The Health Professions Publisher of* Harper and Row, Inc.
East Washington Square, P.O. Box 280, Philadelphia, Pa. 19105

Please enter my subscriptions to the journals checked:

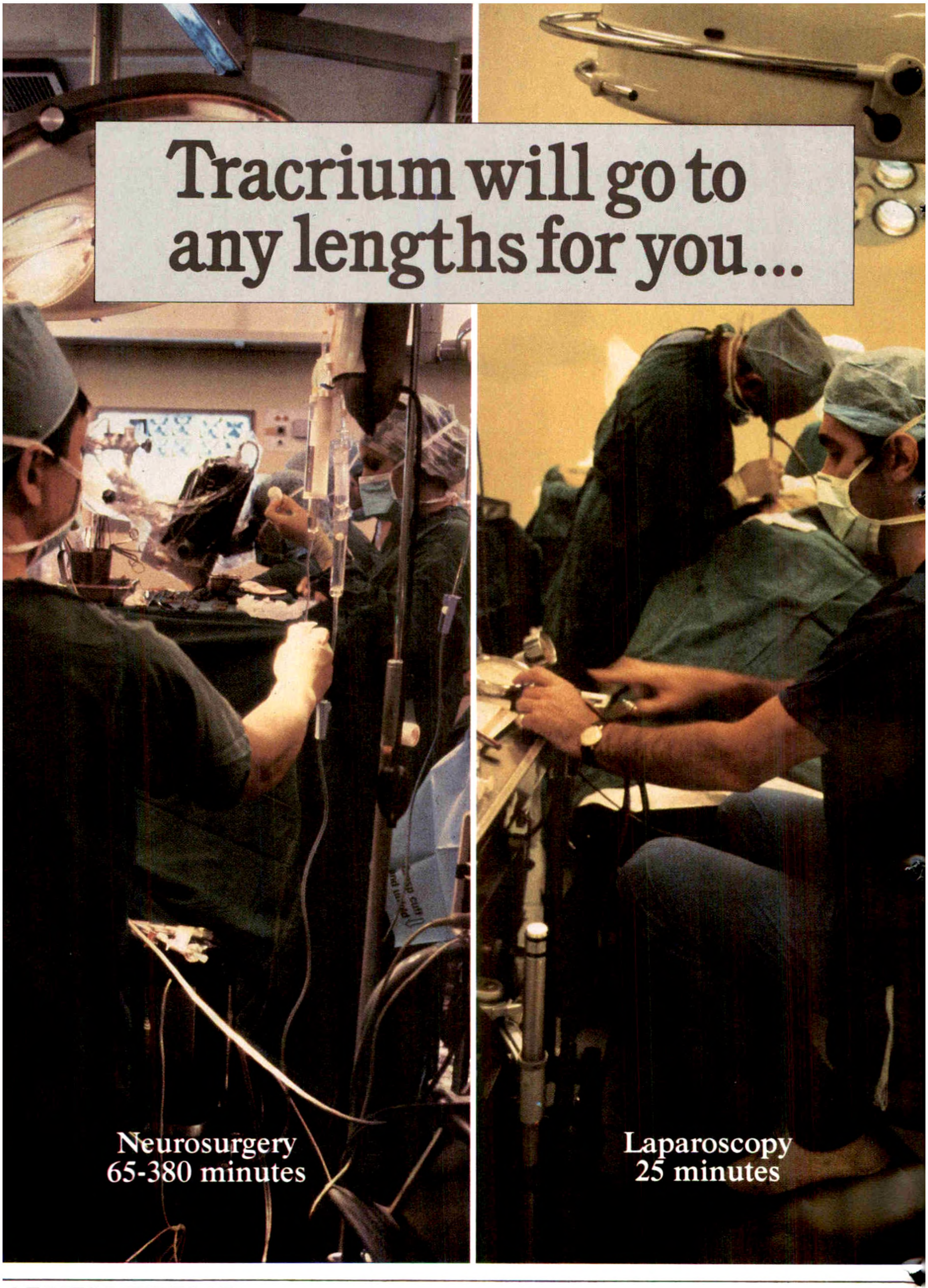
☐ Anesthesiology: Individuals $30 (U.S.). $65 (elsewhere)
☐ Regional Anesthesia: Individuals $35 (U.S.). $40 (elsewhere); Residents $23 (U.S.)
☐ ASA Refresher Courses in Anesthesiology: Individuals $15 (U.S.). $20 (elsewhere)
☐ Please send information on previous volumes of the ASA Refresher Courses

Prices quoted in U.S. funds and subject to change. Orders subject to the approval of Lippincott.

Name ____________
Address ____________
City/State/Zip ____________
My specialty is ____________
☐ Residents: To qualify for special rate, please indicate Hospital and Chief of Staff.
____

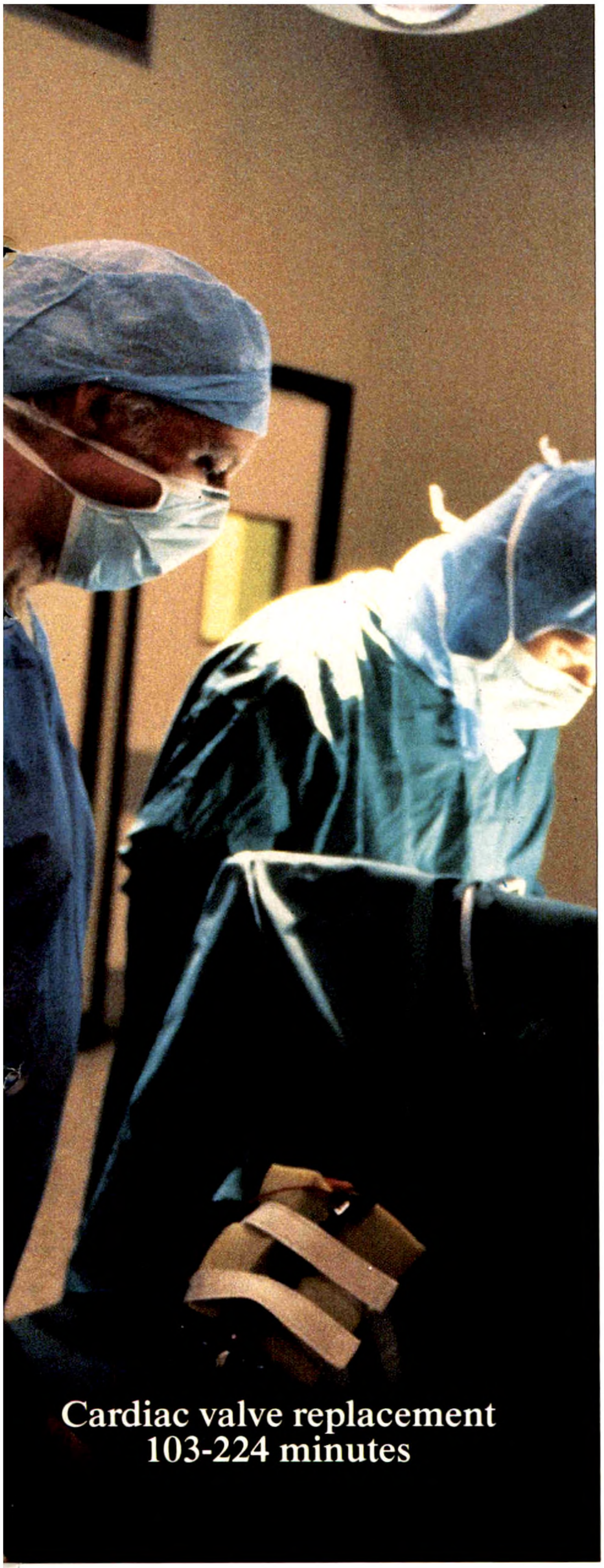
☐ Payment enclosed. Charge: ☐ MasterCard ☐ Visa
☐ Please bill me. ☐ American Express ☐ CHOICE
Card No. ____________
Expiration Date ____________
Signature ____________

348-85
349-85



ALMIC MEDICAL
DIVISION

HE WELLCOME FOUNDATION LTD



Cardiac valve replacement
103-224 minutes

With Tracrium there are no cumulative effects with supplemental dosing, so the pattern of block and recovery remains consistent, regardless of the number of doses given.

Surgical muscle relaxation can therefore be conveniently extended at a uniform level for as long as required, simply by repeated incremental bolus doses given at predictable clock-timed intervals or by continuous i.v. infusion.

The rate of recovery remains just as rapid as that seen after administration of a single bolus dose, so reversal can be promptly and easily achieved whatever the duration of the operation – regardless of the patient's age and hepatic, renal and circulatory status.

All of which adds up to an unusual degree of versatility.

That's why more and more anaesthetists are using Tracrium routinely, in procedures of widely differing type and length, from laparoscopy to open-heart surgery.

Wellcome

Muscle relaxation without cumulation.

TRACRIUM

Atracurium besylate

(Prescribing information overleaf.)

Tracrium Prescribing Information

Uses Tracrium is a highly selective, competitive (non-depolarising) muscle relaxant for use in a wide range of surgical procedures and to facilitate control of respiration. Tracrium is highly suitable for endotracheal intubation, especially where subsequent relaxation is required.

Dosage and administration

Intravenous injection: Adults and children over 1 year: 0.3-0.6 mg/kg depending on the duration of block required; this will provide relaxation for about 15-35 minutes. Tracrium may be used at standard dosage in elderly patients and in those with respiratory, hepatic or renal failure. Full block can be prolonged with supplementary doses of 0.1-0.2 mg/kg as required. Successive supplementary dosing does not give rise to cumulation. Endotracheal intubation can usually be accomplished within 90 seconds of intravenous injection of 0.5-0.6 mg/kg. The neuromuscular block produced by Tracrium can be rapidly and permanently reversed by standard doses of neostigmine which should be preceded by the administration of atropine. Recovery from full block without the use of neostigmine occurs in about 35 minutes.

Continuous infusion: Tracrium is suitable for administration by continuous infusion at rates of 0.005-0.01 mg/kg/minute (0.3-0.6 mg/kg/hour) to maintain neuromuscular block during long surgical procedures. Tracrium maintains acceptable physical and chemical stability in daylight at concentrations of between 0.5 and 0.9 mg/ml at 30°C for up to: 4 hours in: Compound Sodium Lactate Intravenous Infusion B.P.; 8 hours in: Ringer's Injection U.S.P.; Glucose Intravenous Infusion B.P. 5% w/v; Sodium Chloride 0.18% w/v and Glucose Intravenous Infusion B.P. 4% w/v and up to 24 hours in: Sodium Chloride Intravenous Infusion B.P. Tracrium can be administered by infusion during cardiopulmonary bypass surgery, at the recommended infusion rate. Induced hypothermia to a body temperature of 25 to 26°C reduces the rate of inactivation of atracurium, therefore full neuromuscular block may be maintained by approximately half the original infusion rate at these temperatures.

Contra-indications, warnings, etc. Contra-indicated in patients hypersensitive to atracurium besylate. Tracrium should be used with caution in patients receiving aminoglycosides or polypeptide antibiotics and in patients with myasthenia gravis. In common with all other neuromuscular blocking agents, adequate facilities must be available for endotracheal intubation and artificial ventilation. The neuromuscular block produced by Tracrium may be increased by the concomitant use of inhalational anaesthetics such as halothane. Tracrium should not be mixed in the same syringe with any other agent; in particular it must not be mixed with thiopentone or any alkaline agent, as the high pH would cause inactivation of the Tracrium. As with all other neuromuscular blocking agents the possibility of transient hypotension due to histamine release cannot be excluded. Although animal studies have indicated that Tracrium has no adverse effects on foetal development, nevertheless, like all neuromuscular blocking agents, it should be used with caution in pregnant women. Tracrium may be used to maintain neuromuscular relaxation in Caesarean section as atracurium does not cross the placenta in clinically significant amounts.

Presentation Tracrium injection contains 10 mg per ml atracurium besylate. Two ampoule sizes, 2.5 ml and 5 ml, are available.

Basic NHS costs £6.50 for a box of 5 x 2.5 ml ampoules. £12.50 for a box of 5 x 5 ml ampoules. (PL3/0166).

Further information is available on request.

Calmic Medical Division
The Wellcome Foundation Ltd
Crewe, Cheshire

Wellcome

TRACRIUM

Atracurium besylate

CALMIC MEDICAL DIVISION

ACADEMIC PRESS

publishes books and journals in many areas of Science including:

Acoustics, Agriculture, Anatomy, Anthropology, Archaeology, Audiology

Biochemistry, Biology, Botany

Cancer research, Cardiology, Chemistry, Computer science

Economics, Engineering, Environmental science

Food Science

Geography, Geology

Immunology

Materials technology, Mathematics, Microbiology

Neuroscience, Nutrition

Oncology, Ornithology

Pathology, Pharmacology, Physics, Physiology, Psychiatry, Psychology

Religion

Sociology, Speech, Surgery

Toxicology

Virology

Zoology

BOOKS AND JOURNALS

24-28 Oval Road, London NW1 7DX, U.K.
Orlando, FL 32887, USA.

this study which had been initiated by the Association of Anaesthetists and now run by a committee nominated by the Association and by the Association of Surgeons, though subsequently the support of many other bodies had been sought and obtained. Following a preliminary pilot scheme, the main study will begin shortly and will be based on three Regions—the South West, the North and North East Thames Regions. Visits have been made to all the hospitals in these Regions to explain and obtain acceptance for the methods of study. All deaths in hospital within 30 days of an operation will be considered, confidentially, by both surgical and anaesthetic assessors and the final document will be based on these reports. He outlined the problems which had been encountered in the presentation of the previous report on mortality, when adverse comments were initially made in the press. Strenuous attempts will be made to avoid a recurrence of this.

Discussion. Dr Lunn answered numerous questions of detail about the protocol and selection of assessors.

Recovery facilities

Dr R.J. Eltringham (*Gloucester*) reported as Chairman of a Working Party set up by Council to consider recovery facilities. After much discussion in the Working Party and in Council, a document was ready for publication and would be available to members before the end of the year. The document dealt with basic recovery facilities, gave guidelines for good practice in purpose built recovery rooms and made recommendations for the training of nursing staff for recovery room work. The appendix contained a list of drugs found useful in recovery rooms and a short, selected list of useful references.

Discussion. Several linkmen, including Dr F.B. Buckley (*Carlisle*) and Dr R.N. Packham (*Poole*), participated in the discussion. The matters raised included problems met in creating recovery areas in older hospital buildings and the need for anaesthetists to ensure the adequacy of training of nurses who were taking responsibilities for the recovering patient. Particular anxieties were expressed over the use of trainee nurses for this role and the shortages of staff which were encountered in out-of-hours work.

Operating department assistants and their problems

Dr C.A. Foster (*St Thomas' Hospital*) President of the British Association of Operating Department Assistants, reported to the meeting. He noted that the transfer of the ODA grade to the Professional and Technical Staff of the Whitley Council had created almost as many problems as it had been introduced to solve. Many of these difficulties related to the fact that no additional funds had been made available to smooth the transfer, but they were also due to the failure of many Health Authorities to follow the recommendations made in the Advance Letter (PTB 1.84, Appendix A). This stressed the need for full consultation with staff organisations before changes were introduced. He encouraged anaesthetists when they became aware of and wished to help with difficulties in regard to the transfer of ODAs, to become conversant with the PTB handbook.

Dr Foster stressed the position held by the Association, that there was a need for an adequate level of trained and dedicated staff, be they ODAs or nurses.

Discussion. Dr D.W. Eyre-Walker (*Stafford*) expressed the opinion that ODAs should be responsible administratively to consultant anaesthetists or to the Theatre Users Committee and Dr I. McLellan (*Leicester*) also believed they should be taken into anaesthetic departments. It was, however, noted that in its review of the subject, an Association Working Party had stressed the need for a single chain of command in theatre. Dr D.C. Hughes (*Chertsey*) expressed disappointment that not all anaesthetists insisted on having trained assistants with them. Dr Eva M. Kavan (*Bedford*) remarked that although ODAs were preferred by anaesthetists in her region, they were still seen as a threat by some members of the nursing staff. Dr F.B. Buckley (*Carlisle*) expressed his disappointment at the number of ODAs who were available. In spite of the prospect of withdrawal of Faculty recognition, some regions were unable to recruit a sufficient number of trained staff in this grade. Dr M.R. Bryson (*Newcastle*) considered that too much emphasis had been put on the problems of ODAs and this had had an adverse effect on training of nurses. A recent decision in Newcastle to discontinue the Joint Board Clinical Nursing Studies course there was being actively opposed.

Committee on Safety of Medicines

The President, Dr T.B. Boulton, introduced Professor A. Goldberg, Regius Professor of Medicine in Glasgow and Chairman of the Committee on Safety of Medicines (CSM) and said that no drug was entirely safe.

In his opening remarks, Professor Goldberg stated that he welcomed the opportunity to talk about, and to listen to linkmen's opinions on, drug reporting. He reviewed the origins and history of development of drug regulation and the reporting of adverse drug reactions which led to the introduction of the yellow card system by the committee of Safety of Drugs 21 years ago, and the establishment of the CSM in 1971. He stated that this Committee is advisory to the Drug Licensing Authority and that its function is to alert the profession concerning adverse drug reactions and to validate and determine the incidence of such reactions. He described how adverse reactions may occur, emphasising that there is considerable under-reporting of these reactions. A total cf 140,000 adverse reactions have been reported in 21 years; of these, only 124 were related to anaesthetic agents, despite an estimated 3 million anaesthetics being administered per annum. Professor Goldberg presented an analysis of these reports illustrating that thiopentone, halothane, methohexitone and Althesin were the most commonly reported of the general anaesthetic agents, lignocaine of the local anaesthetic agents and atracurium and alcuronium of the neuromuscular blocking drugs. Anaesthesia was, therefore, either very safe or there was under-reporting. During recent years, warnings had been sent out from the CSM to the profession concerning local anaesthetics, halothane and intravenous anaesthetic agents. Professor Goldberg concluded with an account of how the link between increased mortality and the use of etomidate in intensive therapy was established.

Reporting of adverse drug reactions by anaesthetists

Professor J.W. Dundee (*Belfast*), said that although anaesthetists administered more dangerous drugs than most physicians, had a greater knowledge of pharmacology and were in a position to observe drug effects, there was still serious under-reporting of adverse reactions to anaesthetic agents. He went on to discuss the reasons for under-reporting by anaesthetists. These included working alone, a heavy clinical commitment, the use of drug 'side-effects' as part of an anaesthetic technique, the lack of office and secretarial support, logistic difficulties and problems with the yellow card system. In addition, anaesthetists usually have a well-developed instinct for immediate resuscitation and management of drug side-effects, which may, therefore, not be considered important. He questioned whether the yellow card was of an optimum design to be completed by a busy anaesthetist, and stated that a plea for a special card for reporting emergencies in anaesthesia had been rejected. In spite of the difficulties with the yellow card system, much could be done to improve reporting and Professor Dundee suggested that a general awareness of the system should be promoted by making the yellow cards more easily available by informing Theatre Staff and encouraging more involvement with hospital pharmacy departments. Senior anaesthetists should set a peer example and all reactions discussed at local mortality and morbidity meetings should be reported. Publicity, including journal editorials, on the value of reporting by anaesthetists in the assessment of drug toxicity would be valuable in creating and maintaining interest in this matter within the specialty.

Discussion. Dr A. Padfield (*Sheffield*) had reported adverse reactions, but had become disillusioned with the yellow card system and said that there was insufficient time to fill in cards for all common reactions such as histamine release. He agreed that there was under-reporting and recounted examples from his own experience. He commented that some adverse reactions are of late onset and suggested that a special, easy to complete, card should be available to anaesthetists.

Professor Goldberg replied that it was most important to report all severe drug reactions and all adverse reactions, minor or severe, caused by the use of a new drug. He supported involving hospital pharmacists in improving reporting and suggested that yellow cards should be kept on each drug trolley. He considered the yellow card system to be satisfactory if used correctly and was against the creation of special cards. Dr A.J. Whitaker (*Mansfield*) asked whether the CSM's function was to restrict the pharmaceutical industry and to decrease the number of available drugs. Professor Goldberg replied that the CSM was concerned with safety, and its role was not to persecute the drug industry or deprive the community of new drugs. Commenting on remarks made by several linkmen that they had not seen or received yellow cards, Professor Goldberg explained that cards are sent to those who have submitted a report, and added that, in the future, they will be included in NHS prescribing pads and in the British National Formula (BNF). Dr A.B. Leach (*Southampton*) suggested that MIMS and the ABPI data sheet compendium should contain yellow cards. It was pointed out that these were trade publications. Dr A.B. Loach (*Oxford*) asked about telephone reporting and was informed that there was a 24-hour freefone service as outlined in the BNF, page 25. Mr Grimshaw (*CSM*) explained that a yellow card accompanied letters from the CSM. If linkmen were not receiving these letters they should contact the Secretary of the CSM or the Medical Mailing Company. Comments on the adverse reactions to suxamethonium were made by Dr F.B. Buckley (*Carlisle*) and Dr P.W. Winder (*Hull*). Professor Dundee requested that all adverse reactions mentioned at clinical meetings should be reported. Professor Goldberg thanked linkmen for their comments.

Workload for consultant anaesthetists

Dr W.R. MacRae introduced this topic commenting that a considerable number of enquiries from anaesthetists, dealt with by the Secretariat of the Association, were concerned with contract problems. He reviewed the pamphlets which had been produced by the Association on this subject and specifically referred to the latest pamphlet, published in August 1985, relating to the implications of reductions in, or total absence of, junior anaesthetic staff. The guidance outlined in this document has been much more appreciated by the few anaesthetists in consultant-only based departments, a type of service which seemed only to have been introduced in anaesthesia. He said that a reduction in the number of juniors appears essential to improve career prospects for junior anaesthetists and to correct the imbalance existing in the training grades. The impact of such a reduction in junior staff may not yet be fully appreciated. Some anaesthetists are now realising that they have insufficient juniors to provide a satisfactory on-call service in hospitals which have intensive care units and obstetric departments, particularly if these are on more than one geographical site. Dr MacRae emphasised that consultants must not only give good value to the NHS but must also have sufficient time to enjoy the rewards of a career in anaesthesia with the prospect of survival to retirement age and beyond. He concluded by asking for views on the value of the Association's present publications on this topic and invited linkmen to identify special problems and areas on which they would welcome guidance from the Association.

Discussion. Dr J. Duncan (*Dunfermline*) thanked the Association for its support and stated that following Dr MacRae's visit to the consultant establishment in Dunfermline, a consultant-only service, had been increased from 4 to 6 consultants. He recommended the Association workload document to all linkmen and said that the picture of a consultant-only group was not all black and that consultant surgeons could organise their work to advantage on the lines of the Association document. He encouraged the Association to continue producing guidance pamphlets and suggested that increased financial reward may be appropriate for those engaged in a consultant-only service. Dr A. Leslie (*Walsall*) commented that an increase in consultant establishment without junior support, could lead to difficulties with on-call rotas, and requested a balance between juniors and consultants. Dr MacRae replied that there was no possibility of an increase in junior staff and that the only solution was to increase consultant cover. Dr T.B. Boulton stated that the workload must be identified. Dr B. Head (*Bromsgrove*) made the point that only appropriately experienced juniors should be counted in the manpower statistics. Dr MacRae agreed that there may have to be an overlapping of training grades. Dr M.H. Cook (*Ipswich*) reported that he had experienced a lack of applicants for registrar posts and asked if other specialties were reducing junior numbers. Dr MacRae expressed surprise at this lack of applicants and stated that several RHAs have tried to replace registrars in other specialties with consultants. He reminded linkmen that the consultants' contract did not equate with that of a registrar, the more realistic equation being two consultants to replace one registrar. Dr J. Missen (*Chichester*) highlighted the problem of consultant anaesthetists having to work regularly with registrar surgeons. Dr T.B. Boulton replied that traditional patterns of consultant work will have to change.

Secretary's up-date

Dr M. Inman thanked linkmen for attending the meeting and also for their letters to the secretariat over the past year. He stated that many of the queries raised had been included in the agenda for the meeting.

The International Relations committee continues to promote anaesthesia in the Third World and anaesthetists interested, or able to help in this work, should contact Dr R.J. Eltringham (*Gloucester*) chairman of this committee. Offers of surplus anaesthetic equipment for the Third World would be gratefully received by: ECHO, The Joint Mission Hospital Equipment Board Ltd, Ullswater Crescent, Coulson, Surrey CR3 2HR. (Tel: 01 660 2220).

Books and journals will be shipped, free of charge, to the developing countries by: Ranfurley Library Service, Kensington Barracks, Kensington Church Street, London W8 (Tel. 01 937 5234).

The various awards given by the Association for travel and research were detailed. Recently, Council had agreed to increase the travel grant to a maximum of £500, and to the introduction of a new award of up to £1000 to help with funding of educational visits to Third World countries. The Association Research Fellowship had been adjusted and applicants from departments in District General Hospital were being encouraged. The Association pamphlet on fees for Private Practice last reviewed in January 1984, will be up-dated in January 1986. Dr Inman reported that the Anaesthetic Department at Northwick Park wished to hear of cases of hepatitis occurring in anaesthetists.

Open forum

Tenure of registrar posts

Dr M. Marshall (*Newcastle*) considered that the Registrar numbers were too large and that tenure of under 2½ years did not give optimum experience, particularly to those with FFARCS. Dr MacRae agreed and thought 4 years as a maximum more realistic, and numerically a 6-year period could be seen. Dr P.A.D. Williams (*Brighton*) questioned the need for such a prolonged period of registrar training. In reply, Dr MacRae said that promotion to Senior Registrar was the stumbling block, a view supported by Dr J.F. Searle (*Exeter*).

Short-listing procedures

Dr C.J. Barham (*East Grinstead*) suggested that Juniors should not visit departments before being short-listed for a post, and that all applicants should be so informed. This view was supported by Dr P.A.D. Williams (*Brighton*) and Dr M. Marshall (*Newcastle*) on logistic grounds. Dr T.B. Boulton confirmed that the Junior Group were considering this matter and a document would be available in the near future.

Grading of anaesthetic secretaries

Dr B.R. Whittard (*Torquay*) asked the Association for guidance on improving remuneration for anaesthetic department secretaries by supporting promotion to the

Higher Clerical or General Administrative Grade. Dr T.B. Boulton said that there had been a DHSS Working Party on this issue, and that he had achieved some success locally. Dr D.C. Hughes (*Surrey*) and Dr J.E. Goodwin (*York*) reported success in up-grading secretaries; this depended heavily on providing evidence on the level of responsibility and administrative duties undertaken.

Contra-indications to epidurals

If the midwife/patient ratio was not one-to-one, Dr J. Jenkins (*Great Yarmouth*) was unwilling to undertake epidural analgesia. Dr M.R. Bryson (*Newcastle*) commented that an epidural service exposed deficiencies which should be publicised. The national shortage of midwives was stressed by Dr T.H.L. Bryson (*Liverpool*), who suggested that the English National Board should be made aware of the situation regarding epidural services.

Withdrawal of heavy nupercaine

Dr R.M.C. Hodgson (*Plymouth*) asked if the Association could exert pressure to prevent the withdrawal of this drug. Dr T.B. Boulton confirmed that approaches to the manufacturing company had been made, without success. Dr P. Lee (*Preston*) pointed out that amethocaine was a satisfactory alternative drug.

Separation of anaesthetists' and surgeons' fees

Dr A. Padfield (*Sheffield*) urged the Association to proceed with this matter. He was assured that separation of fees was Association policy. However, there were both disadvantages and advantages to this strategy.

Management of intensive care units

The question of who should be in administrative charge of ICU's in the future was asked by Dr M.R. Bryson (*Newcastle*). In discussion, the opinion was expressed that a suitably qualified anaesthetist, physician, or surgeon could perform this function.

Consultant anaesthetists to service surgical registrar lists

Dr T.D. McGhee (*London*) asked whether consultants should anaesthetise for surgical registrars on a permanent basis. In discussion, it was stated that a consultant could exert more effective control of these lists.

Lack of consultation between the specialty and the drug industry

Dr A.J. Whitaker (*Mansfield*) emphasised that this lack of consultation was also evident with equipment and said that anaesthetists, being the consumers, could influence companies. Dr T.B. Boulton replied that the Association had been able to exert influence on companies with success in some instances.

Regionalisation of specialties

Views were sought by Dr R. Kavan (*Oakley*) concerning the effect on training in districts where there had been regionalisation of some surgical services. In reply, this was considered to be a Faculty matter.

Study leave for junior staff

Dr B.M. Dempsey (*Hounslow*) expressed anxiety on reports that expenses for Juniors' study leave were not being honoured.

The meeting was concluded by the President, Dr T.B. Boulton, who thanked linkmen for their useful and informed comments.

Notice to contributors to *Anaesthesia*

Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Articles accepted become copyright of *Anaesthesia*.

Contributors are requested to submit two copies of manuscripts. They are also advised to retain a third copy as the Editors cannot accept responsibility for the loss of manuscripts in the post. The covering letter should be signed personally by all the authors and careful consideration should be given to the decision to include more than five authors. Articles should be forwarded to:

Dr J. N. Lunn, Editor of ***Anaesthesia****, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.*

PREPARATION OF MANUSCRIPTS

Articles for *Anaesthesia* should be prepared in accordance with *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1**: 532–5) except that the titles of journals in the reference section should be given in full (see below). A reprint of these requirements of which this notice is a summary, can be obtained from the *British Medical Journal* price 50 pence (U.K.).

Type manuscripts on white bond paper, 20.3 × 26.7 cm or 21.6 × 27.9 cm (8 × 10½ in. or 8½ × 11 in.) or ISO A4 (212 × 297 mm) with margins of at least 2.5 cm (1 in.). Use double, and preferably triple, spacing throughout, including the references. Please do not use a dot matrix printer, particularly one with poor quality descenders or ascenders. Unseparated, fan-folded manuscripts may be returned to the author.

The manuscript should consist of the following sections in this order each beginning on a new page: *title page*, *summary* and *key words*, *text*, *acknowledgments*, *references*, *individual tables*, and *legends for figures*.

Number pages consecutively, beginning with the title page. Type the page number in the upper right-hand corner of each page.

THE TITLE PAGE

The name of the author and the address to which proofs and other correspondence is to be addressed should appear in the top left-hand corner of the sheet.

The main title should be restricted to five words if this is possible. It should be typed in capitals across the centre of the title page.

A subsidiary title of not more than 12 words may be supplied if this is considered to be necessary. This should be typed in lower case immediately beneath the main title.

The names of the authors should be typed IN CAPITALS across the title page immediately beneath the titles without degrees or designations. Initials should precede the surname. One forename may be given in full according to the author's preference. If there is more than one author the word 'AND' should be placed before the name of the last author.

A line should be typed across the title page below the author(s) name(s) in capitals.

The author(s) name(s) degrees and designations should be typed in lower case below the line. Initials and/or forename should precede the name of each author and his degrees, without full stops between letters, and appointment (e.g. Consultant, Registrar, etc.) should follow it.

A full postal institutional address should follow the names, degrees and appointments. Correspondence will normally be addressed to the first author but, if it is desired to direct correspondence other than to the first author, or if different authors belong to different institutions or departments, a separate sentence should be added; this should start on a new line and begin 'Correspondence should be addressed to ...' and a full postal address should follow.

SUMMARY AND KEY WORDS

Start a new sheet

The second page should carry a summary of not more than 150 words. The summary should state the purpose of the study or investigation, basic procedures, main findings and their statistical significance, and the principal conclusions.

Do not use abbreviations except for units of measurement (e.g. mg, cm, etc.).

Key (indexing) words. Below the abstract, provide and identify as such, three to 10 key words or short phrases that will assist indexers. Use terms from the Medical Subject Headings list from *Index Medicus*. The Editor may modify these at proof stage to conform with agreed practice of certain other anaesthetic journals in the English language.

COPYRIGHT OFFPRINTS

Authors submitting a manuscript do so on the understanding that if it is accepted for publication, exclusive copyright in the paper shall be assigned to the Association. In consideration for the assignment of copyright, the Publisher will supply 25 offprints of each paper. Further offprints may be ordered at extra cost; the copyright assignment form and the offprint order form will be sent with the proofs. The Association will not put any limitation on the personal freedom of the author to use material contained in the paper in other works.

(continued overleaf)

THE TEXT

Start a new sheet

The text of observational and experimental articles, case reports, etc. is usually divided into sections with the headings *Introduction*, *Methods*, *Results* and *Discussion*. Long articles will need subheadings within some sections to clarify their content.

Letters for the correspondence pages should be double spaced and prepared in accordance with the format in a recent copy of *Anaesthesia*.

Headings: three steps of heading may be used in typescripts:

(i) CAPITALS across the centre of the page.
(ii) Underlined words
These should be typed at the left hand side of the page above the paragraph which they precede.
(iii) Underlined words at the beginning of a paragraph. These may either be followed by a full stop or form part of the first sentence of the paragraph.

ACKNOWLEDGMENTS

Start a new sheet

Acknowledge those who have made substantive contributions to the study or the preparation of the manuscript. Authors are responsible for obtaining written permission for publication of reproduced figures and tables from authors and publishers and from everyone acknowledged by name because of copyright conventions and because readers may infer their endorsement of the data and conclusions.

REFERENCES

Start a new sheet

Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by arabic numerals. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. Use double or treble space typing.

Use the form of reference adopted by the U.S. National Library of Medicine and used in *Index Medicus*. Use the style of the examples cited at the end of this section.

The titles of journals should be given in full.

Avoid using abstracts as references except those published in a recognised journal. 'Unpublished observations' and 'personal communications' may not be used as references, although references to written, not verbal, communications may be inserted (in parentheses) in the text. Include among the references manuscripts accepted but not yet published; designate the journal followed by (*in press*) in parentheses. Information from manuscript submitted but not yet accepted should be cited in the text as (unpublished observations) in parentheses.

The references must be verified by the author(s) against the original documents.

Examples of correct form of references

Note: first and last pages in all references.

JOURNAL

Standard journal article—(List all authors)

Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294:** 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

Osler AG. *Complement: mechanisms and functions.* New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. AMA drug evaluations. 3rd ed. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

Rhodes AJ, Van Rooyen CE, *comps. Textbook of virology; for students and practitioners of medicine and other health sciences.* 5th ed. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

Weinstein L, Swartz MN Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease.* Philadelphia: WB Saunders, 1974: 457–72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, Md: National Center for Health Statistics, 1972. (*Vital and health statistics. Series* **10:** Data drom the National Health Survey, No. 69) [DHEW publication No. (HSM) 72-1036].

OTHER ARTICLES

Newspaper article

Shaffer RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

Roueche B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

TABLES

Do not include tables in the text. Start a new sheet for each table and space the material adequately. The author(s) name(s) should appear in the top right-hand corner.
Indicate the approximate position of each table in relation to the subject matter of the text in the right-hand margin of the appropriate page on the manuscript. Do not submit tables as photographs. Number tables consecutively with arabic numerals. Supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes. Explain in footnotes all non-standard abbreviations that are used in each table. For footnotes, use the following symbols in this sequence: *, †, ‡, §, ||, ¶, **, ††, etc. Identify statistical measures of variations such as SD and SEM. *Legends for tables* should appear on the face of the table.

Cite each table in the text in consecutive order and mark the approximate position of the table in the right-hand margin of the text.

FIGURES

Each figure should be separate. Do not include figures in the text but collect together in an envelope or folder.
Indicate the approximate position of each figure in relation to the subject matter of the text in the right-hand margin of the appropriate page of the manuscript. Drawings, charts and diagrams should be submitted in black indian ink on a smooth white card and should be about twice the size of that desired in the published version with no lettering. Full plate, glossy black and white photographs will be accepted if they are sufficiently clear. All letters and numerals required on the face of figures must be clearly typed or written on tracing paper firmly attached with self-adhesive tape to the back of the figure and folded over from the front as a cover. They will then be printed in the style of *Anaesthesia* in the exact location indicated. Identify each figure by its sequential number in pencil on the reverse of the illustration and include the title of the paper and the authors' names. Mark the top of the illustration on the reverse by an arrow and the word 'Top'.
All sources of identification of patients must be removed.

LEGENDS FOR FIGURES

Start a new sheet
Type legends for illustrations double spaced with arabic numerals corresponding to the illustrations. When symbols, arrows, numbers or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

CONVENTIONS AND ABBREVIATIONS

Statistics and measurements should be given in figures except that numerals one to nine should be in words if not followed by a measurement symbol (e.g. 'two patients' but '2.0 mg'). The *Système International* (SI) will usually be used except that vascular pressures will be recorded in mmHg and cmH$_2$O. Imperial measurements will not be used except in an historic context. The 24 hour clock will be used.

Contributors are advised to study the SI *Conversion Tables* provided in the January 1978 issue of *Anaesthesia*, *Units, Symbols and Abbreviations* (*A Guide for Biological and Medical Editors and Authors*) published by the Royal Society of Medicine, London W1M 8AE, and *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1**: 532–5).

LETTERS FOR PUBLICATION

Should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University of Wales Hospital, Heath Park, Cardiff CF4 4XW, UK.

Letters should be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters above. The degrees and diplomas of each author must be given in a covering letter which must be signed personally by all the authors.

Correspondence presented in any other style or format may be the subject to considerable delay and may be returned to the author for revision.

The editors regret that failure to comply with the above requirements may result in a delay in publication of accepted papers.

REVIEW JOURNALS

This journal is covered by *Current Contents*, *ASCA* and the *Science Citation Index*.

Contents: Anaesthesia, vol. 41, no. 4, April 1986

EDITORIAL

Adverse reactions to drugs and anaesthetists
J.W. Dundee 351

ORIGINAL ARTICLES

Vecuronium induced neuromuscular blockade. The effect of increasing dose on speed of onset
W.R. Casson and R.M. Jones 354
A pre-induction test dose for suxamethonium
J. Carnie 358
An investigation of factors affecting postoperative rewarming of adult patients
F. Carli, M. Gabrielczyk, M.M. Clark and V.R. Aber 363
Obstetric anaesthetic services in Scotland in 1982
D.B. Scott and R.E.G. Aitken 370
Atracurium infusions in patients with renal failure on an ITU
R.B. Griffiths, J.M. Hunter and R.S. Jones 375
Profound atracurium induced neuromuscular blockade. A comparison of evoked reversal with edrophonium or neostigmine
W.R. Casson and R.M. Jones 382
Changes in skin thermal clearance during anaesthesia
J.L. Saumet, C .. Degoute, A. Dittmar and V. Banssillon 386
The effect of halothane on cerebral electrical activity. An assessment using the cerebral function analysing monitor (CFAM)
K.J. Wark, P.S. Sebel, C. Verghese, D.E. Maynard and S.J.W. Evans 390

CASE REPORTS

Anaesthesia for congenital analgesia. A case report
P.R. Layman 395
Raynaud's phenomenon precipitated by blood transfusion
J.K. Moore and D.W. Proctor 398
Accidental spinal anaesthesia following intrathoracic intercostal nerve blockade. A case report
M.R.J. Sury and R.M. Bingham 401
Carcinoid syndrome with myasthenia gravis. An unusual and interesting case
S.J. Keens, M.J. Desmond and J.E. Utting 404
Multiple complications after internal jugular vein catheterisation
Z. Gamulin, J.-C. Brückner, A. Forster, F. Simonet and J.-C. Rouge 408

APPARATUS

The digital control of anaesthetic gas flow
R.W. Boaden and P. Hutton 413

FORUM

The use of antacids as a prophylaxis against Mendelson's syndrome in the United Kingdom. A survey
B. Sweeney and I. Wright 419
Intravenous feeding with medium chain triglycerides. Effect on blood gases and the complement system in critically ill patients
M.J. Ball and J.W. Sear 423

CORRESPONDENCE 427

ANAESTHETIC LITERATURE 447

NEWS AND NOTICES 454

THE ANNUAL CONFERENCE OF LINKMEN OF THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND, 1985 464

Printed in Great Britain by Fletcher & Son Ltd, Norwich

Acc.
25.9.87

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain & Ireland

Volume 41 Number 5 May 1986

LIBRARY

Published for
The Association of Anaesthetists of Great Britain and Ireland by
Academic Press Grune & Stratton
London Orlando San Diego New York Austin
Boston Sydney Tokyo Toronto

ISSN 0003–2409

Solcotrans®
...the new, sim
and effective w
# of transfusin
autologous blo

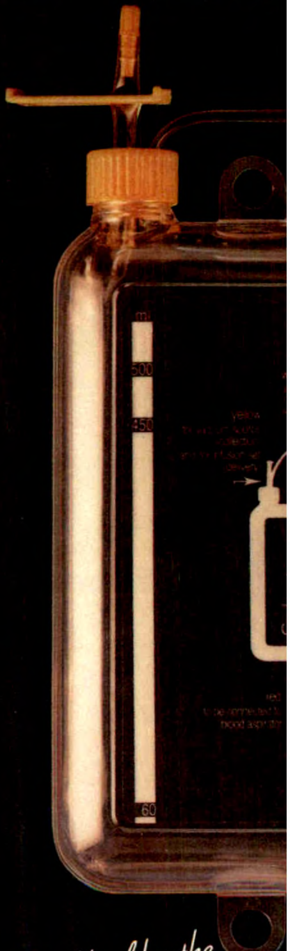
SOLCOTRANS is a sterile, hand-held, disposable device for the intra-operative collection and re-infusion of autologous blood.
The design permits the same unit to be used for collection and administration. The surgeon can collect blood via linkage with a vacuum source. The anaesthetist uses SOLCOTRANS as a blood bag – adding a blood filter and administration set.

Indications
- aortic aneurysm and other vascular procedures
- abdominal surgery (ruptured liver, liver resection, ruptured spleen)
- trauma with intrathoracic, intra abdominal or retroperitoneal bleeding.

Contra-indications blood should not be retrieved from the following areas:
- septic
- infected
- malignant tumour tissue
- open intestinal

- SOLCOTRANS returns blood to the patient within minutes.
- SOLCOTRANS saves bank blood.
- Avoids the risk of donor infection.
- Is cost effective.

SOLCOTRANS is available sterilised and ready to use. If you would like further information on SOLCOTRANS please telephone or write to:



The best blood for the patient is his own!

Cabot Limited
Cabot Ltd, Copyground Lane, High Wycombe HP12 3HE. Tel: 0494 34991/2

Cabot Limited is a subsidiary
Solco Basle Ltd. Switzerland

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

---

Editorial Board
Editor J. N. LUNN
Assistant Editors M. MORGAN, C. E. BLOGG, R. GREENBAUM, R. M. JONES
Chairman P. J. HELLIWELL
Advisory Editors R. S. ATKINSON, T. B. BOULTON
Members C. F. SCURR, P. J. F. BASKETT, D. J. HATCH and a representative of the Junior Anaesthetists Group
Ex officio
The President of the Association T. B. BOULTON
The Honorary Treasurer of the Association M. M. BURROWS
The Honorary Secretary of the Association M.T. INMAN
The Assistant Honorary Secretary of the Association P. MORRIS

Editor Emeritus C. LANGTON HEWER

Sub-editors of special sections
L. KAUFMAN Anaesthetic literature
A. PADFIELD National and local events
G. D. PARBROOK Audiovisual reviews
M. J. HARRISON Computer programs
JACQUELINE WELCH, DIANE WINTERBURN Reference librarians
D. V. BATEMAN Honorary proof reader

Address for literary contributions Dr J. N. Lunn, The Editor, *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK [telephone Cardiff (0222) 763601; Ansafone available].

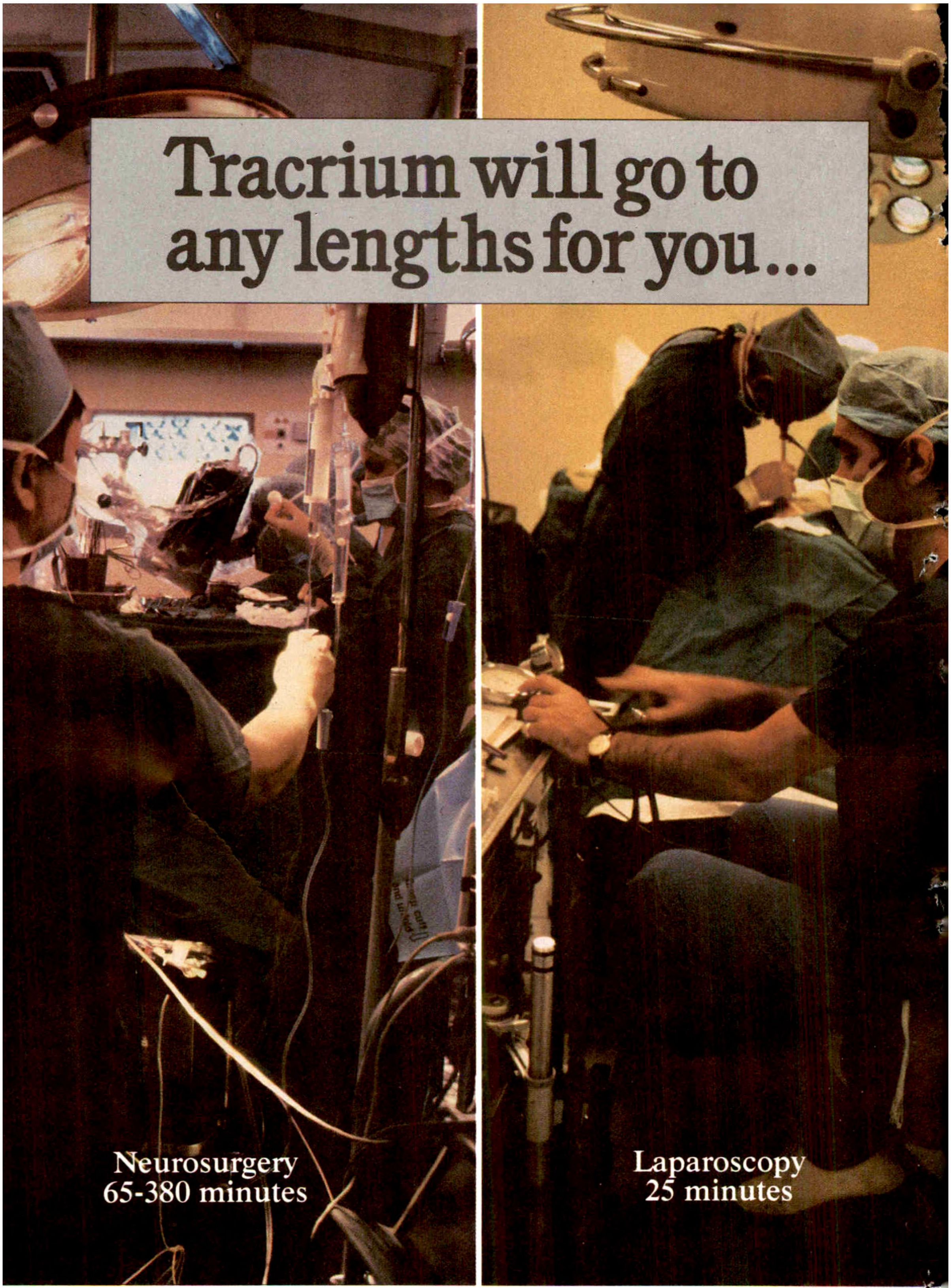
Neither the Editor nor the Association of Anaesthetists of Great Britain and Ireland is in any way responsible for the statements made or the views expressed by contributors.
Investigations performed on man must conform to appropriate ethical standards including voluntary consent and acceptance by an ethical committee.

Published monthly (January–December) at 24–28 Oval Road, London NW1 7DX, England by Academic Press Inc. (London) Limited for the Association of Anaesthetists of Great Britain and Ireland, Rooms 475–478, Tavistock House South, Tavistock Square, London WC1H 9LG. As from December 2nd 1985, 9 Bedford Square, London WC1B 3RA.
1986, Volume 41, 12 issues. Inland £80.00 inclusive of postage and packing; abroad, $189.00 inclusive of postage and packing. Subscription orders should be sent to Academic Press Inc. (London) Limited, High Street, Foots Cray, Sidcup, Kent DA14 5HP (Tel. 01-300-0155). Send notices of change of address to the office of the Publishers at least 6–8 weeks in advance. Please include both old and new addresses.
Application to pay at second class postage rates pending at Jamaica, New York 11431, U.S.A.
Air freight and mailing in the U.S.A. by Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, U.S.A.

© 1986 The Association of Anaesthetists of Great Britain and Ireland. The appearance of the code at the bottom of the first page of a paper in this journal indicates the copyright owner's consent that copies of the paper may be made for personal or internal use, or for the personal or internal use of specific clients in the U.S.A. This consent is given on the condition, within the U.S.A., that the copier pay the stated per-copy fee through the Copyright Clearance Center Inc., 27 Congress Street, Salem, MA 01970, U.S.A. for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, for resale or for copying or distributing copies outside the U.S.A.

ISSN 0003-2409

LIBRARY
UNIVERSITY



ALMIC MEDICAL
DIVISION
E WELLCOME FOUNDATION LTD

Cardiac valve replacement
103-224 minutes

With Tracrium there are no cumulative effects with supplemental dosing, so the pattern of block and recovery remains consistent, regardless of the number of doses given.

Surgical muscle relaxation can therefore be conveniently extended at a uniform level for as long as required, simply by repeated incremental bolus doses given at predictable clock-timed intervals or by continuous i.v. infusion.

The rate of recovery remains just as rapid as that seen after administration of a single bolus dose, so reversal can be promptly and easily achieved whatever the duration of the operation – regardless of the patient's age and hepatic, renal and circulatory status.

All of which adds up to an unusual degree of versatility.

That's why more and more anaesthetists are using Tracrium routinely, in procedures of widely differing type and length, from laparoscopy to open-heart surgery.

Wellcome

Muscle relaxation without cumulation.

TRACRIUM

Atracurium besylate

(Prescribing information overleaf.)

Tracrium Prescribing Information

Uses Tracrium is a highly selective, competitive (non-depolarising) muscle relaxant for use in a wide range of surgical procedures and to facilitate control of respiration. Tracrium is highly suitable for endotracheal intubation, especially where subsequent relaxation is required.

Dosage and administration

Intravenous injection: Adults and children over 1 year: 0.3-0.6 mg/kg depending on the duration of block required; this will provide relaxation for about 15-35 minutes. Tracrium may be used at standard dosage in elderly patients and in those with respiratory, hepatic or renal failure. Full block can be prolonged with supplementary doses of 0.1-0.2 mg/kg as required. Successive supplementary dosing does not give rise to cumulation. Endotracheal intubation can usually be accomplished within 90 seconds of intravenous injection of 0.5-0.6 mg/kg. The neuromuscular block produced by Tracrium can be rapidly and permanently reversed by standard doses of neostigmine which should be preceded by the administration of atropine. Recovery from full block without the use of neostigmine occurs in about 35 minutes.

Continuous infusion: Tracrium is suitable for administration by continuous infusion at rates of 0.005-0.01 mg/kg/minute (0.3-0.6 mg/kg/hour) to maintain neuromuscular block during long surgical procedures. Tracrium maintains acceptable physical and chemical stability in daylight at concentrations of between 0.5 and 0.9 mg/ml at 30°C for up to: 4 hours in: Compound Sodium Lactate Intravenous Infusion B.P.; 8 hours in: Ringer's Injection U.S.P.; Glucose Intravenous Infusion B.P. 5% w/v; Sodium Chloride 0.18% w/v and Glucose Intravenous Infusion B.P. 4% w/v and up to 24 hours in: Sodium Chloride Intravenous Infusion B.P. Tracrium can be administered by infusion during cardiopulmonary bypass surgery, at the recommended infusion rate. Induced hypothermia to a body temperature of 25 to 26°C reduces the rate of inactivation of atracurium, therefore full neuromuscular block may be maintained by approximately half the original infusion rate at these temperatures.

Contra-indications, warnings, etc. Contra-indicated in patients hypersensitive to atracurium besylate. Tracrium should be used with caution in patients receiving aminoglycosides or polypeptide antibiotics and in patients with myasthenia gravis. In common with all other neuromuscular blocking agents, adequate facilities must be available for endotracheal intubation and artificial ventilation. The neuromuscular block produced by Tracrium may be increased by the concomitant use of inhalational anaesthetics such as halothane. Tracrium should not be mixed in the same syringe with any other agent; in particular it must not be mixed with thiopentone or any alkaline agent, as the high pH would cause inactivation of the Tracrium. As with all other neuromuscular blocking agents the possibility of transient hypotension due to histamine release cannot be excluded. Although animal studies have indicated that Tracrium has no adverse effects on foetal development, nevertheless, like all neuromuscular blocking agents, it should be used with caution in pregnant women. Tracrium may be used to maintain neuromuscular relaxation in Caesarean section as atracurium does not cross the placenta in clinically significant amounts.

Presentation Tracrium injection contains 10 mg per ml atracurium besylate. Two ampoule sizes, 2.5 ml and 5 ml, are available.

Basic NHS costs £6.50 for a box of 5 x 2.5 ml ampoules. £12.50 for a box of 5 x 5 ml ampoules. (PL3/0166).

Further information is available on request.

Calmic Medical Division
The Wellcome Foundation Ltd
Crewe, Cheshire

Wellcome

TRACRIUM

Atracurium besylate

CALMIC MEDICAL DIVISION

ACADEMIC PRESS

publishes books and journals in many areas of Science including:

Acoustics, Agriculture, Anatomy, Anthropology, Archaeology, Audiology

Biochemistry, Biology, Botany

Cancer research, Cardiology, Chemistry, Computer science

Economics, Engineering, Environmental science

Food Science

Geography, Geology

Immunology

Materials technology, Mathematics, Microbiology

Neuroscience, Nutrition

Oncology, Ornithology

Pathology, Pharmacology, Physics, Physiology, Psychiatry, Psychology

Religion

Sociology, Speech, Surgery

Toxicology

Virology

Zoology

BOOKS AND JOURNALS

24-28 Oval Road, London NW1 7DX, U.K.
Orlando, FL 32887, USA.

LAERDAL SILICONE MASKS

for Anaesthesia, Resuscitation and Respiratory Therapy

IMPORTANT FEATURES

Transparent domes
Easy monitoring of lip colour and presence of vomitus.

Contoured pliable mask rims
Airtight and comfortable seal with a minimum of pressure.

Small external measurements
Easy to hold even for operators with small hands. Comfortable grip reduces hand fatigue.

Soft mask port bushings
Quick and safe attachment to gas delivery equipment. Will adapt to the small variations often found in connector diameter and tapering.

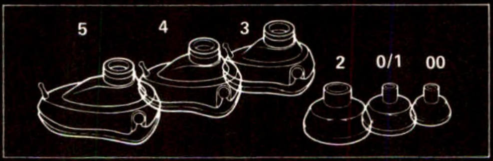
SUPERIOR ECONOMY

Can be re-used hundreds of times
Hard polysulfone and soft silicone parts will accept all commonly used methods of disinfection and sterilization, including pasteurization, boiling, gas sterilization and steam autoclaving up to 136°C (277°F).

Can be stored almost indefinitely
Materials and manufacturing provide extremely long shelf life.

All-purpose suitability
allows standardization in purchasing, inventory and cleaning.

FULL RANGE OF SIZES



Large adult (5), small adult (4), child (3) masks have rigid domes and soft rims and mask port bushings. Infant sizes (00, 0/1, 2) are made in one soft silicone rubber piece.

Laerdal Medical Ltd.
TRAINING AIDS and MEDICAL EQUIPMENT

Laerdal Medical Limited
Laerdal House
Goodmead Road
Orpington
Kent BR6 0HX
Tel. Orpington: (0689) 76634
Telex: 8955251 LML G

UNIVERSITY OF WALES

Department of Anaesthetics, University of Wales College of Medicine, and Department of Business Administration, University of Wales Institute of Science and Technology.

MANAGEMENT FOR ANAESTHETISTS
22nd–25th July 1986

Course Directors:
M. D. Vickers, M.B., B.S., F.F.A.R.C.S., Professor of Anaesthetics, University of Wales College of Medicine.

R. Mansfield, M.A., Ph.D., Professor of Business Administration, U.W.I.S.T.

This three-day residential course covers the administrative structure of the N.H.S. and the doctor's role within it, resolution of conflict, industrial relations, decision making, scheduling, interview techniques, N.H.S. financial methods, committee management and medical organisations relevant to anaesthetists.

National and local experts will conduct the sessions, which will include small discussion groups.

Further details and application forms available from:

Margaret Thomas (Mrs.), Dept. of Anaesthetics, University of Wales College of Medicine, Heath Park, Cardiff. Tel: (0222) 755944 Ext. 3108.

Pocket Spirometer

- ☐ **INEXPENSIVE**
- ☐ **ACCURATE**
- ☐ **PORTABLE**
- ☐ **PEAK FLOW**
- ☐ **FEV$_1$**
- ☐ **FVC**

Now Available with Printer Output for Hardcopy of Data and Volume Time Curve using the new Micro Medical Instruments Pocket Printer.

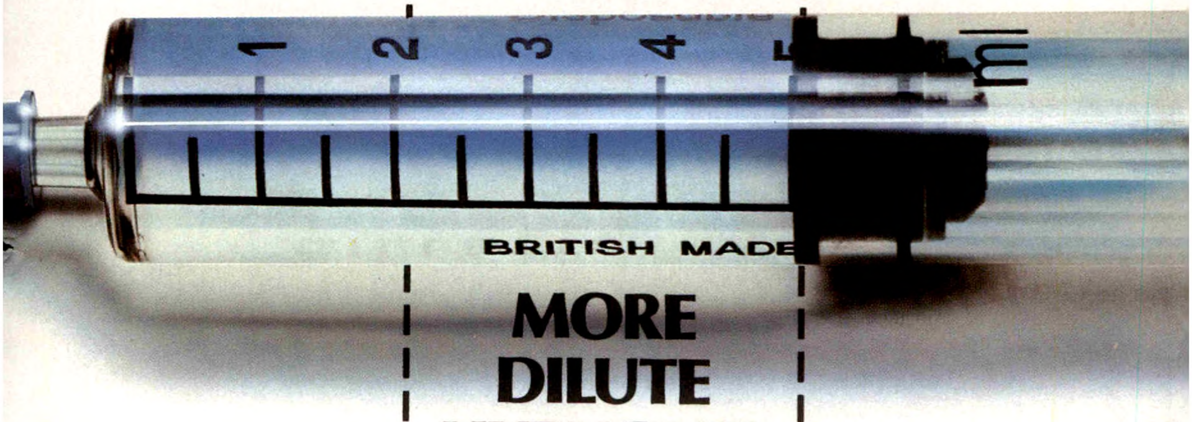
The Unique *Hand Held* Spirometer

For more information on the Micro Medical Instruments Pocket Spirometer and our other respiratory products contact:-

micro Medical Instruments

Micro Medical Instruments,
P.O. Box 6, Rochester, Kent.
ME1 2AZ, ENGLAND.
Telephone: Medway (0634) 712290

WE'VE GIVEN YOU PRECISELY WHAT YOU WANTED



MORE DILUTE HYPNOVEL

When we asked how Hypnovel could be improved, many users asked for a more dilute presentation, so that finer control of dosage, and therefore sedation, could be achieved. So the 2ml presentation was joined by an ampoule containing the same 10mg of midazolam, but in 5ml of solution. The extra 3ml of diluent makes it simpler to obtain the full benefits of Hypnovel. Proven benefits of Hypnovel include fast onset and rate of recovery, excellent amnesia and minimal venous complications.[1]

THE HYPNOVEL 10mg/5ml AMPOULE

midazolam

FOR MORE PRECISE CONTROL OF I.V. SEDATION

Prescribing Information

Indications Intravenous sedative cover. Alternative intravenous agent for induction of anaesthesia in high-risk patients. Intramuscular premedication. **Dosage and Administration** *Intravenous sedation* Usual total dose 2.5mg to 7.5mg (approx. 0.07mg/kg body-weight). *Intravenous induction of anaesthesia* Unpremedicated patients: 0.3mg/kg body-weight or more. Premedicated patients: 0.2mg/kg body-weight may be adequate. *Intramuscular premedication* (10mg/2ml ampoule only) Usual dose about 5mg (approx. 0.07-0.1mg/kg body-weight). Elderly patients are more sensitive to the effects of Hypnovel and lower doses should be used. Children over the age of seven years may receive Hypnovel for induction of anaesthesia in a dose of 0.15mg/kg body-weight. **Contra-indications** Benzodiazepine sensitivity; acute pulmonary insufficiency; respiratory depression. **Precautions** Use during pregnancy and lactation should be avoided. Patients should not drive or operate machinery for eight hours after administration. Avoid alcohol. Sedative effects of other centrally-acting drugs may be intensified. For the administration of Hypnovel a second person should always be present and facilities for resuscitation should always be available. **Side-effects** Hypnovel is well tolerated and changes in arterial blood pressure, heart rate and respiration are usually slight. The rapid injection of a high dose can induce soft-tissue airway obstruction or apnoea of short duration. Local effects on veins are infrequent. However, pain on injection and thrombophlebitis may occur. **Presentation** Ampoules containing 10mg midazolam base as the hydrochloride in 5ml or 2ml aqueous solution, in packings of 10. **Basic NHS Cost** 76p per 10mg/5ml ampoule. 64p per 10mg/2ml ampoule. **Product Licence Numbers** 0031/0189 (10mg/5ml), 0031/0126 (10mg/2ml). **Product Licence Holder** Roche Products Limited, PO Box 8, Welwyn Garden City, Hertfordshire AL7 3AY. **Reference** 1. Anaesthesia. 1982, **37**, 1002.
Hypnovel is a trade mark.

ROCHE

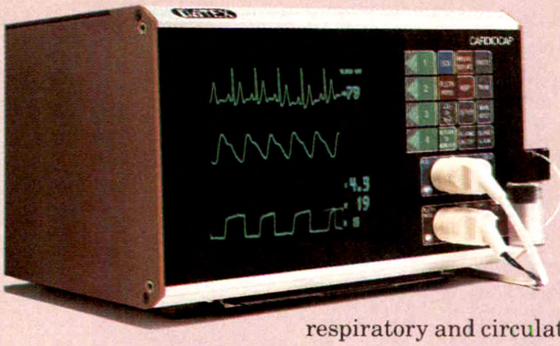
Two breath taking advan
from Vickers Medical

Vickers Medical maintains its position at the forefront of patient monitoring systems with the launch of two outstanding new anaesthetic monitors – Cardiocap and Multicap. Both units incorporate the most sophisticated innovations in sensor and microcomputer technology. They are compact, cost-effective and versatile, and greatly enhance the efficiency of the operating theatre and recovery room.

MULTICAP

This is the newest addition to the Vickers Medical range of respiratory gas monitors. Multicap is simple to operate and economical to run. Its sampling system is controlled by microprocessors which guarantee reliable operation, while its six displays give you simultaneous, at-a-glance data on essential physiological functions.

- **Miniature sensors – unique to Vickers Medical – have ultra-fast response time which allows "breath-by-breath" measurement of CO_2, N_2O and O_2**
- **Easy use of communications capabilities guaranteed by complete software control**
- **Audio and visual alarms on major parameters monitored**
- **Sensor requires no servicing**



CARDIOCAP

This integrated non-invasive monitor is unique in that, as a single unit, it displays all the vital respiratory and circulatory information you need at a glance.

- **ECG**
- **Digital heart rate**
- **Breath-by-breath CO_2, O_2 and N_2O**
- **Integral, non-invasive blood pressure wave-form and digital value**
- **Plethysmographic Pulse/Invasive Blood Pressure Wave-Form**
- **Two temperature channels**
- **Complete communication capability**

For further information, contact
Nick Tyrrell, Product Manager,
Vickers Medical, Priestley Road,
Basingstoke, Hampshire,
England RG24 9NR.
Telephone 0256-29141.
Telex 858697. FAX 0256460802

Vickers
Medical

Cardiocap and Multicap are registered trademarks of Instrumentarium Corporation and are manufactured in Finland by Datex.

Anaesthesia monitoring at its most advanced

UNIVERSITY HOSPITAL OF WALES CARDIFF

Residential Course on

INTENSIVE CARE

2nd, 3rd July, 1986

This course is of interest to trainee candidates for higher diplomas and Consultants with Intensive Care interest.

Guest Lecturer:
Dr. D. Ryan, Freeman Hospital, Newcastle-upon-Tyne

Speakers include:
Professor M. D. Vickers Professor M. Rosen Dr. Colin Wise

Course fee:
£80 (non-residential) £130 (residential)

Further details and application forms available from:
Dr. Judith M. Davies, Department of Anaesthetics, University of Wales College of Medicine, Heath Park, Cardiff, CF4 4XW

Telephone No: **Cardiff 755944, Extn. 3107**

Joint Anaesthesiology Update

One day Anglo-American Symposium
Day Case Anaesthesia
Post-operative Analgesia

Chairmen:
John T. Herbert, MD
Medical Director of Ambulatory Surgery and attending Anesthesiologist, Manhattan Eye, Ear & Throat Hospital, New York.

Michael Harmer, FFARCS
Consultant Anaesthetist, University Hospital of Wales, Cardiff.

London, 17th September, 1986

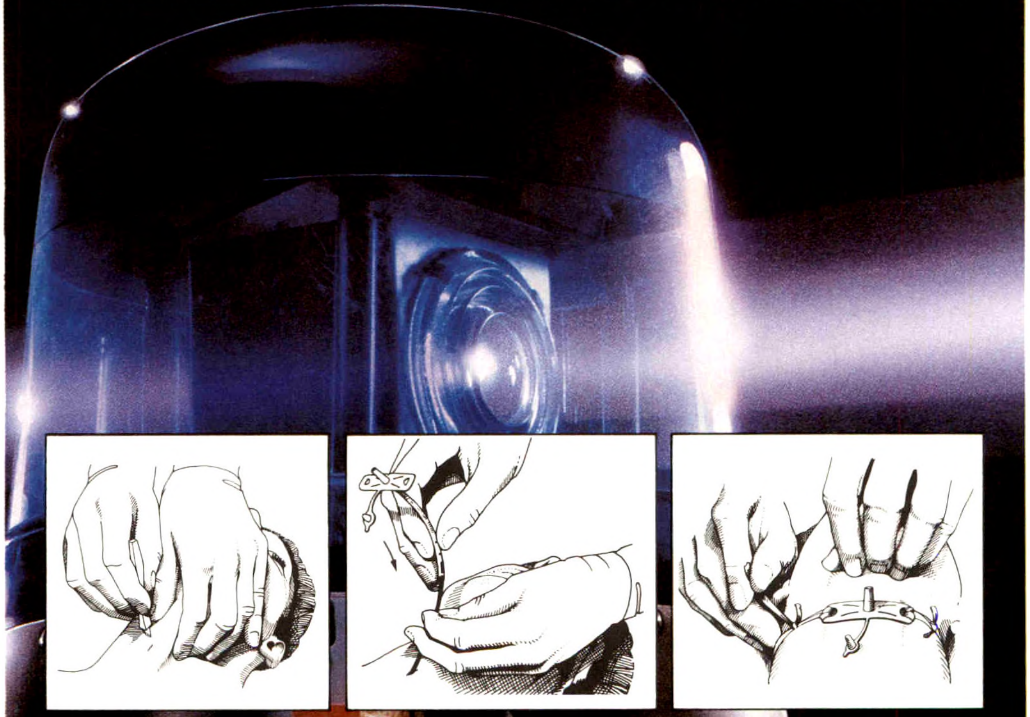
Information from:
Anglo-American Symposium Secretary, c/o Department of Anaesthetics, University Hospital of Wales, Cardiff, CF4 4XW.

WHEN BREATHING IS DIFFICULT ......

AND TIME IS SHORT

.... Mini-Trach II CAN

SIMPLY SAVE A LIFE



PORTEX

PORTEX LIMITED, Hythe, Kent, England, CT21 6JL
Tel: Hythe (0303) 66863 & 60551. Telex: 96165.
Facsimile: (0303) 66761

sims A Smiths Industries Medical Systems Company

1984

ribing
nation

ation
e relaxation
gical and
thetic procedures.
ge Response is
le, but as a guide:
s: 0.20-0.25mg/kg
enously for approximately 20-30 minutes'
tion, 0.30mg/kg for approximately
nutes' relaxation. Children: 0.125 to
/kg bodyweight. **Contra-indications**
rsensitivity to alcuronium, myasthenia
; myasthenic (Eaton-Lambert) syndrome.
utions Dosage requirements may be
d in renal impairment, hepatic and
muscular diseases, and by concomitant use
ibiotics of the polymixin and
glycoside groups, volatile anaesthetics,
with local anaesthetic properties,
ion-blockers, electrolytes (Mg, Na, K, Ca).
during pregnancy. **Side-effects**
tension and, less frequently, tachycardia.
cases of anaphylactoid reaction have been
led. **Presentation** Ampoules containing
alcuronium chloride in 2ml packings of 10.
NHS Cost Alloferin ampoules 10mg x 10,
Licence Number 0031/5000
rin is a trade mark.
of preparation April 1986.

In both short and prolonged surgery
A single dose of Alloferin (0.20-0.25mg/kg) provides muscle relaxation for approximately 20-30 minutes[2] and a 0.30mg/kg dose gives about 40 minutes of relaxation. The relaxation can be maintained for longer procedures with "no noticeable accumulation" of Alloferin[3] and the number of repeat doses required is similar to that with tubocurarine or pancuronium[4]

Considerable cardiovascular stability
Alloferin allows blood pressure and heart rate to be kept within acceptable limits in most patients due to lack of marked histamine-releasing, ganglion-blocking or vagolytic actions[2,5,6]

Easy reversal for uncomplicated recovery
Alloferin has been found to be easier to reverse with neostigmine than either pancuronium or tubocurarine[4]

---

ences 1. Brit.J.hosp.Med.,1980,*23*,153.
.Chir.Gynaec.,1977,*66*,113. 3. Europ.J.clin.
acol.,1980,*17*,449. 4. Anesth.Analg.
es.,1971,*50*,926. 5. Int.Anesth.Clins,1979,
6. Brit.J.Pharmacol.,1980,*70*,501.

A useful
muscle-relaxant
for routine use[1]

ALLOFERIN

ALCURONIUM

CHE
Roche Products Limited
PO Box 8 Welwyn Garden City
Hertfordshire AL7 3AY

Anaesthesia, 1986, Volume 41, pages 469–471

Editorial

C. Langton Hewer, MB, BS, FFARCS, MRCP, DA

By kind permission of the Editor of the *St Bartholomew's Hospital Journal and the Department of Medical Photography of St Bartholomew's Hospital.*

Christopher Langton Hewer, Editor Emeritus of *Anaesthesia* and Consulting Anaesthetist to St Bartholomew's Hospital, London, died on 28 January 1986 in his ninetieth year. He was successively Founder Editor (1946–1966), Advisory Editor (1966–1976) and Editor Emeritus (1976–1986). His death thus brings to an end an association with this journal which has extended over 40 years from the preparation of the first issue in 1946 to the present.

Dr Hewer qualified in medicine from St. Bartholomew's Hospital Medical College in 1918; in so doing he followed in the footsteps of his grandfather, father and great uncle. It is of interest that the latter relative, John Langton, held the unique St Bartholomew's post of 'Administrator of Chloroform' from 1865 to 1868.[1] Dr Hewer's career as a clinical anaesthetist, innovator, teacher and prominent figure in the dramatic scientific and political development of the specialty of anaesthesia in the last half century, has recently been extensively reviewed in the medical[2,3] and lay[4,5] press; naturally in the circumstances, however, his own fascinating account of his first experience of the administration of anaesthetics as a medical student in 1917 in his Hewitt Lecture of 1959[6] has not been recalled. It makes compelling reading and vividly describes the situation, one year after the death of Hewitt, before continuous flow anaesthetic machines were available. The standard techniques at that time were ether or chloroform administered on the open mask, by the Clover or Hewitt inhaler, or by the Junker vaporizer.

Hewer's first experience of early continuous flow oxygen, nitrous oxide and ether anaesthesia was in the Royal Army Medical Corps in the closing year of the First World War under the tutelage of Dr Torrance Thompson of Edinburgh, who owned one of the original American Gwathmey machines.[1,6] Hewer returned to St Bartholomew's in 1919 on demobilisation and, such was the rapidity of promotion in those days, that after 6 months as Resident Anaesthetist, he was appointed to the staff of the Hospital as an 'Administrator of Anaesthetics' at the early age of 24. He was soon to be involved with the continuous flow technique again when he was associated with Dr H.E.G. Boyle in the development of

0003–2409/86/050469 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

his modification of the Gwathmey apparatus, the forerunner of the commonest type of anaesthetic apparatus in use in the United Kingdom to this day. Dr Hewer was, from then on, involved in almost every innovation in anaesthetic practice in the years between the two World Wars, and most particularly in the fields of thoracic and toxic thyroid surgery. He was also responsible, early in the 1939–1945 War, for reintroducing and developing the use of trichloroethylene as an alternative to flammable ether and potentially dangerous chloroform.[6]

The academic and political life of the specialty of anaesthesia was necessarily much more limited during the nineteen twenties and thirties than it is now, because the number of specialist anaesthetists was small and anaesthesia was largely in the hands of general practitioners outside the big centres. Hewer participated actively in the business of the organisations concerned with anaesthesia, however. He frequently took part in the discussions of the Section of Anaesthetics at the Royal Society of Medicine and served as both its Honorary Secretary and its President. He also became President of the Anaesthetic Section of the British Medical Association and was a founder member of the Association of Anaesthetists of Great Britain and Ireland, and an examiner for the Diploma of Anaesthetics which was introduced in 1935.[7]

It was, however, the imminence of the introduction of the British National Health Service which stimulated a quickening of the pulse of organised anaesthesia in the United Kingdom.[8] The need was to establish anaesthesia as a clearly defined specialty before the 'appointed day', so that anaesthetists would be given equal status with consultants of other disciplines. The establishment of this journal *Anaesthesia* in 1946,[9] at a time when the fortunes of the only contemporary United Kingdom journal for anaesthetists were at a low ebb, was a part of this momentum which led ultimately to the founding of the Faculty of Anaesthetists of the Royal College of Surgeons of England, at the instigation of the Association.[10] Dr Langton Hewer was one of 21 Foundation Fellows of the Faculty. His appointment as Editor of *Anaesthesia* was an obvious choice. His *Advances in Anaesthesia and Analgesia* (which was first published in 1932 and which ultimately ran to its 14th edition under his direction in its fiftieth year in 1982) was already a widely acclaimed work in its 5th edition; he had published two text books *Anaesthesia for Children* (1922) and, in conjunction with Dr Boyle, *Practical Anaesthetics* (1923) and a number of articles; and he wrote almost effortlessly with a pleasing clarity and style.

Dr Hewer's reign as Editor of *Anaesthesia* lasted 20 years.[11] He had Dr Blair Gould as a sub-editor, but there was no secretarial assistance and, to the end of Hewer's Editorship, all correspondence was typed by the Editor on his own rather ancient typewriter—and yet the journal always arrived on time on the first day of the quarter! Hewer's editorials were an important feature of the journal throughout the 20 years. He wrote 75 out of the 80 which were printed between 1946 and 1966 and contributed a 76th to the 30th anniversary issue in 1976.[12] These crisp, well written contributions give a fascinating account of the scientific and political development of the United Kingdom specialty over these exciting years. Each new development and issue was examined carefully and its advantages and disadvantages or pros and cons fairly discussed, before a thoughtful conclusion was drawn.

Dr Hewer had the reputation for being conservative in his professional clinical outlook in later years, but this is an oversimplification. His aim at all times was safety during anaesthesia. The motto of the Association (*In somno securitas*) might have been written for him, and many famous patients, including Royalty, Winston Churchill and Bernard Shaw, benefitted from his meticulous care. His approach to every innovation was cautious but analytical. If he concluded that it would be advantageous he welcomed it—as, for instance, was the case with halothane[13] and external cardiac massage.[14] If, however, he scented danger (as he did in the case of paralysis and controlled ventilation for abdominal surgery),[15] he stuck to his tried and practised techniques or attitudes. His philosophy is well demonstrated in his last monograph *Thoughts on modern anaesthesia* (1970).

Christopher Langton Hewer was a physically tall man who towered intellectually above many of his contemporaries in his and other specialties. He was, however, despite his apparently paradoxical penchant for fast cars, a quiet and intimate person who preferred to exert an influence from the background and with his pen, rather than to engage in face to face confrontation. He was kind and considerate to his many associates and trainees, who held him in deep respect and affection, and he treated their indiscretions with tolerance salted with dry humour.

Deafness afflicted him in his latter years and led to a reluctance to attend public functions, and a further cause of sadness was the death of his devoted wife Phœbe 7 years before his own. The photograph which accompanies this Editorial also headed the moving appreciation in the *St Bartholomew's Hospital Journal* by Dr Frankis Evans (Hewer's colleague, friend and foil over many years) on the occasion of his retirement from National Health Service practice in 1961. It shows him as he was then, still Editor of *Anaesthesia* and still fully in possession of his very considerable intellectual powers. It is thus that we, who knew and worked with him (and we are sure also his family of two sons and one daughter), would wish to remember this great man to whom we owe so much.

Association of Anaesthetists of Great Britain and Ireland,
9 Bedford Square,
London WC1B 3RA

T.B. BOULTON

References

1. EVANS FT. Christopher Langton Hewer. An Appreciation. *St. Bartholomew's Hospital Journal* 1961; **65:** 147–8.
2. *Obituary. British Medical Journal* 1986; **292:** 490.
3. *Obituary. Lancet* 1986; **1:** 455.
4. *Obituary. The Daily Telegraph* 1986; 31 January: 14.
5. *Obituary. The Times* 1986; 1 February: 10.
6. HEWER CL. Forty years on. Frederic Hewitt Lecture. *Anaesthesia* 1959; **14:** 311–30.
7. *Editorial. Anaesthesia* 1948; **3:** 1.
8. *Editorial. Anaesthesia* 1948; **3:** 44.
9. *Editorial. Anaesthesia* 1946; **1:** 1.
10. *Association News. Anaesthesia* 1948; **3:** 129–30.
11. *Editorial. Anaesthesia* 1966; **21:** 323.
12. HEWER CL. Editorial. *Anaesthesia* 1976; **31:** 1023–4.
13. *Editorial. Anaesthesia* 1957; **12:** 371.
14. *Editorial. Anaesthesia* 1962; **17:** 1.
15. *Editorial. Anaesthesia* 1964; **19:** 477.

Editorial notices

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

News and Notices sections

The first issue of each quarter will contain full News and Notices sections.

Copy dates for these will be: 13 June 1986 for October 1986, 12 September 1986 for January 1987, and 12 December 1986 for April 1987.

Supplementary News and Notices sections will be published in other issues but they will contain only material which requires publication before the next full News and Notices section.

Anaesthesia, 1986, Volume 41, pages 472–476

Single breath induction of anaesthesia, using a vital capacity breath of halothane, nitrous oxide and oxygen

N. C. T. WILTON AND V. L. THOMAS

Summary

Inhalational induction of anaesthesia, using a single vital capacity breath of 4% halothane in 66% nitrous oxide and 33% oxygen was evaluated in 100 unpremedicated outpatients. The technique was found to be acceptable to most (91%) of the patients studied, with a mean (SD) induction time (measured from beginning of inspiration to loss of 'eyelash reflex') of 83(21) seconds. Relative cardiovascular stability was a notable finding of the technique, with a slight decrease in the mean arterial pressure of only 10%. Anaesthetic induction time was unaffected by age, weight or smoking habits. The technique of single breath induction is therefore proposed as a safe and acceptable alternative to intravenous induction in co-operative adult patients.

Key words
Anaesthetic techniques; induction.
Anaesthetics, volatile; halothane.

Inhalational induction of anaesthesia is seldom used in routine adult practice because the long induction time is unacceptable to both the patient and the anaesthetist. There is also the potential for a prolonged excitement phase with the risks of laryngospasm and vomiting, although these problems are seldom seen during inhalational induction using halothane in paediatric practice.

It has been suggested that a single breath induction using halothane and oxygen in volunteers,[1] decreases induction time when compared with conventional inhalational induction techniques.[2] The addition of nitrous oxide to the inhaled mixture will decrease the concentration of halothane required to induce anaesthesia,[3] thus shortening the induction period, and will minimise the cardiovascular depression that tends to occur with halothane–oxygen anaesthesia.[4,5]

We have evaluated a single breath induction technique using nitrous oxide, halothane and oxygen in an unpremedicated group of surgical outpatients, to determine whether the technique may be used as a safe and acceptable alternative to intravenous induction.

Method

One hundred ASA class I and II patients over

N.C.T. Wilton, MRCP, FFARCS,* Registrar, V.L. Thomas, MB, ChB, FFARCS Registrar, Shackleton Department of Anaesthetics, Level E, Centre Block, Southampton General Hospital, Shirley, Southampton SO9 4XY.

*Present address: Department of Anesthesiology, University of Michigan Medical Center, Ann Arbor, Michigan 48109, U.S.A.

0003–2409/86/050472 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

the age of 16 years who presented for minor outpatient surgery under general anaesthesia were studied. Informed consent for the study, which was approved by the hospital ethical committee was obtained at the pre-operative visit. All patients were unpremedicated.

Monitoring was commenced on arrival in the anaesthetic room. The electrocardiograph was displayed continuously and the arterial blood pressure measured at minute intervals using a microprocessor-controlled automatic oscillotonometer (either Dinamap or A.S.D.I. Sentry). A 3-G 'Butterfly' needle was inserted in the dorsum of the right or left hand before the induction was started. Prior to induction, a Mapleson A breathing system with a 4-litre reservoir bag was prepared and filled with a mixture of 4 per cent halothane in 66% nitrous oxide and 33% oxygen, supplied by 6 litres/minute fresh gas flow. Two control readings of blood pressure and heart rate were obtained before the induction sequence was started. The patient was then instructed to 'breathe in deeply and then breathe out as far as possible' (i.e. to exhale to residual volume). The anaesthetic system and mask were then gently applied to the patient's face, and the patient instructed to 'breathe in as far as possible and hold your breath' (i.e. a vital capacity breath).

The duration of apnoea, induction time and any excitatory phenomena were recorded by a separate observer. Induction time was recorded as the time interval between the beginning of the vital capacity breath and the disappearance of the eyelash reflex. When the eyelash reflex had disappeared, the inspired halothane concentration was reduced from 4 per cent to 3 per cent and after a further 2 minutes again reduced to 2 per cent.

The patient was left undisturbed for 5 minutes after induction, during which time blood pressure and heart rate were measured at one minute intervals and any dysrhythmias noted. All patients were visited approximately 1–2 hours after anaesthesia by the author who had not been responsible for the induction, and asked a series of questions from a prepared questionnaire, about their recall and opinion of the induction.

Statistical analysis on the obtained data was performed using unpaired and paired *t*-tests, plus linear regression analysis as appropriate.

Table 1. Demographic data of 100 patients studied

	Mean	Range	SD
Age (years)	54.3	17–90	18.5
Weight (kg)	68.9	50–108	13.2

Table 2. Duration of apnoea and induction time during single breath induction

	Mean	Range	SD
Duration of apnoea (seconds)	32	5–90	22
Induction time (seconds)	83	40–150	21

Results

The demographic data of the study group are shown in Table 1. The mean durations of apnoea, and induction times are shown in Table 2. There was neither correlation between duration of apnoea and induction time, nor did changes in age or weight affect either of the previous variables, as shown in Table 3. Duration of apnoea and induction time were also unaffected by smoking habits, (Table 4). Cardiovascular measurements before, during and after induction are summarised in Table 5, and the changes in mean arterial pressure and heart rate are shown graphically in Fig. 1. The incidence and nature of excitatory phenomena observed during induction are shown in Table 6.

Table 3. Correlation coefficients for age and weight versus apnoea and induction time

	Correlation coefficient (*r*)	Significance
Apnoea versus induction time	0.18	N.S.
Age versus apnoea	0.17	N.S.
Age versus induction time	0.15	N.S.
Weight versus apnoea	<0.1	N.S.
Weight versus induction time	0.21	N.S.

Table 4. Comparison of apnoea and induction times in seconds, mean (SD) for smokers and non-smokers

	Smokers $n = 41$	Non-smokers $n = 59$	Significance
Period of apnoea	30 (17)	34 (24)	NS
Induction time	81 (27)	84 (34)	NS

Table 5. Changes in cardiovascular variables during induction. Values, means (SD)

	Time (minutes)						
	Before induction		After induction				
	−1	−2	1	2	3	4	5
Systolic B.P. (mmHg)	147	148	139	135	131	130	128
	(22)	(26)	(23)	(25)	(23)	(23)	(22)
Diastolic B.P. (mmHg)	83	82	80	79	77	75	74
	(15)	(15)	(14)	(16)	(15)	(14)	(15)
Mean B.P. (mmHg)	103	102	98	95	94	92	92
	(17)	(19)	(17)	(18)	(18)	(16)	(18)
Heart rate (beats/minute)	76	78	85	81	75	71	68
	(16)	(16)	(18)	(17)	(15)	(15)	(15)
Number of patients with dysrhythmias							
Atrial	2	3	2	3	3	5	4
Ventricular	4	4	3	5	4	5	4

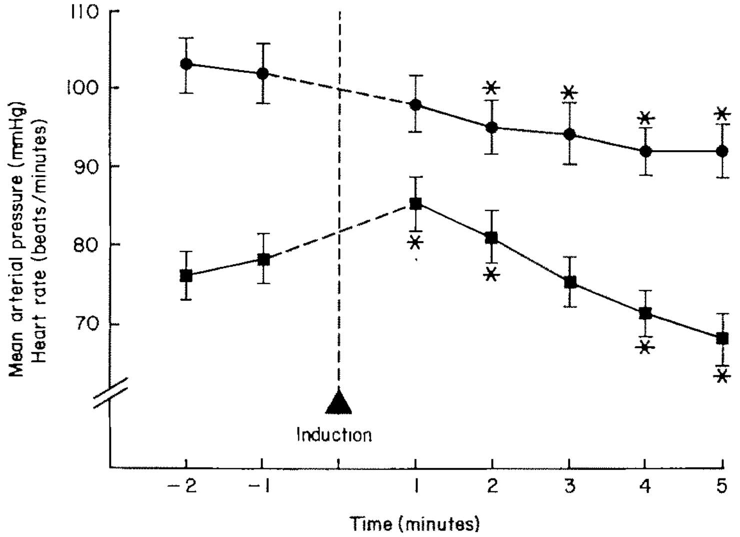


Fig 1. Changes of mean arterial pressure (MAP) and heart rate (HR) during single breath induction, ●, MAP; ■, HR; *, $p<0.01$ (Mean: 2 × SEM).

From the postoperative questionnaire, all patients could recall the induction sequence as far as the vital capacity breath and then breath holding; other information from the questionnaire is shown in Table 7. Of the 89 patients who had had a previous anaesthetic, 82 received an intravenous induction, and of these, 74 (90%), were prepared to undergo single breath induction again.

Table 6. Incidence of excitatory phenomena observed during induction

Excitatory phenomena	% incidence
Movement	6
Coughing	7
Hiccough	1

Discussion

This study shows that inhalational induction of anaesthesia using a single breath technique

Table 7. Results from questionnaire (100 patients)

	Yes	No
Do you remember holding your breath?	100	0
Do you remember the smell of the gas?	87	13
Did you find it—pleasant 7		
—no comment 51		
—unpleasant 29		
Did you get any ringing or buzzing in your ears?	17	83
Would you have this form of anaesthetic again?	91	9
Have you had an anaesthetic before?	89	11

is a safe and acceptable method for use in cooperative adult patients. To achieve anaesthesia by the inhalational route, sufficient concentration of the anaesthetic agent must be present in the brain, which, in the steady state correlates with the minimum alveolar concentration (MAC).[6] The inspired concentrations of inhalational agent during induction need to be much higher than the MAC of that agent, due to the rapid uptake of that agent during induction,[7,8] which tends to lower the alveolar concentration. Furthermore, a large gradient exists between the inspired and alveolar concentration during induction, which will be greater with the more soluble halothane than with nitrous oxide.[9] For these reasons, high concentrations (4 per cent) of halothane were used during induction. The addition of nitrous oxide further tends to increase the speed of induction, since, used in the high concentrations, it significantly decreases the concentration of halothane required to induce anaesthesia.[3] Furthermore, the high concentration of nitrous oxide tends to increase the relative concentration of halothane in the alveoli, so augmenting its uptake by the second gas effect.[10,11] By exhaling to residual volume and then inhaling to vital capacity, the maximum quantity of anaesthetic agent enters the lungs and hence reaches the alveoli in one breath. Using a mixture of nitrous oxide and halothane, it then does not matter if the patient fails to sustain a vital capacity breath. If the patient continues to breath hold, although the fractional concentration of nitrous oxide will tend to fall due to its initial uptake, that of halothane will tend to rise,[11] whereas if the patient starts to breathe, the alveolar concentration of nitrous oxide will tend to approach the inspired concentration and the halothane concentration will also tend to be increased.[10] As would then be expected, there was no correlation seen between duration of apnoea and the time for induction. Hypoxia does not occur using this technique because a vital capacity breath with an inspired oxygen of 33 percent will provide more than sufficient oxygen for the period of apnoea. Furthermore, the concentrating effect of nitrous oxide will ensure that the fractional concentration of oxygen tends to increase during the period of apnoea.

The lack of correlation between age and induction time may be due to the decrease in MAC that occurs with age,[12] this is offset by the slower rate of increase in alveolar concentration that also occurs with age.[13] Smoking did not affect the induction time, although theoretically the ventilation–perfusion mismatching that occurs in these patients might be expected to prolong the induction period.[14] Using halothane, which is relatively soluble, as well as nitrous oxide, minimises the impact of ventilation–perfusion abnormalities.[14]

Relative cardiovascular stability was a notable finding with the single breath induction, despite the high initial concentrations of halothane and the mild Valsalva manoeuvre that tends to accompany a vital capacity breath. The mild decrease in blood pressure, although statistically significant ($p < 0.01$), is of doubtful clinical significance, and is of similar magnitude to that seen with slow intravenous induction using barbiturates.[15,16] The relative bradycardia observed after 5 minutes is not usually a feature of halothane anaesthesia,[5,17] although it has been reported previously;[18,19] again, this did not cause any clinical problems.

Some excitatory phenomena occurred during induction (as shown in Table 5) but there was no patient recall, neither was there any evidence of more serious excitatory phenomena, vomiting or laryngospasm. One patient who exhibited movement had to be physically restrained but did not recall the event. The mean induction time (as measured from the beginning of inspiration to loss of eyelash reflex) of 83 seconds was acceptable to most patients since 91 per cent were content to undergo this form of induction again. Loss of consciousness occurred well before the loss of eyelash reflex, as few patients remembered exhaling their vital capacity breath.

The induction time using the single breath technique is slightly longer than that seen with intravenous agents,[20] but there is less delay in achieving a satisfactory anaesthetic concentration of the inhalational agents for maintenance of anaesthesia. This is because the respiratory depression, or apnoea that may accompany intravenous induction delays the subsequent rate of rise of the alveolar concentration of inhaled agents, whereas with the inhalational route, for the reasons already stated, the patient will continue to take up the anaesthetic agent even during apnoea.

In summary, we suggest that a single breath induction technique using 4 percent halothane in nitrous oxide and oxygen is a safe, acceptable and practical alternative to intravenous induction in cooperative, unpremedicated, adult patients. The speed of induction appears unaffected by age, weight or smoking habits.

Acknowledgments

The authors would like to express their gratitude to Dr D. Saunders for advice regarding the statistical analysis of the results, and Mary Blackmore for secretarial assistance in the preparation of this manuscript.

References

1. Ruffle JM, Latta WB, Snider MT. Single breath halothane oxygen induction in man. *Anesthesiology* 1982; **57:** A461.
2. Ruffle JM, Snider MT. Onset of hypnosis with halothane induction using single breath, triple breath and conventional techniques. *Anesthesiology* 1984; **61:** A498.
3. Saidman LJ, Eger EI II. Effect of nitrous oxide and of narcotic premedication on the alveolar concentration of halothane required for anesthesia. *Anesthesiology* 1964; **25:** 302–6.
4. Hornbein TF, Martin WE, Bonica JJ, Freund FG, Parmentier P. Nitrous oxide effects on the circulatory and ventilatory responses to halothane. *Anesthesiology* 1969; **31:** 250–60.
5. Bahlman SH, Eger EI II, Smith NT, Stevens WC, Shakespeare TF, Sawyer DC, Halsey MJ, Cromwell TH. The cardiovascular effects of nitrous oxide–halothane anesthesia in man. *Anesthesiology* 1971; **35:** 274–85.
6. Eger EI II. *Anesthetic uptake and action.* Baltimore: Williams and Wilkins, 1974; 1–2.
7. Severinghaus JW. The rate of uptake of nitrous oxide in man. *Journal of Clinical Investigation* 1954; **33:** 1183–9.
8. Mapleson WW. The rate of uptake of halothane vapour in man. *British Journal of Anaesthesia* 1962; **34:** 11–8.
9. Eger EI II. *Anesthetic uptake and action.* Baltimore: Williams and Wilkins, 1974; 77–96.
10. Epstein RM, Rackow H, Salanitre E, Wolf GL. Influence of the concentration effect on the uptake of anesthetic mixtures: The second gas effect. *Anesthesiology* 1964; **25:** 364–71.
11. Stoelting RK, Eger EI II. An additional explanation for the second gas effect: a concentrating effect. *Anesthesiology* 1969; **30:** 273–7.
12. Gregory GA, Eger MD, Munson ES. The relationship between age and halothane requirement in man. *Anesthesiology* 1969; **30:** 488–91.
13. Eger EI II, Bahlman SH, Munson ES. The effect of age on the rate of increase of alveolar anaesthetic concentration. *Anesthesiology* 1971; **35:** 365–72.
14. Eger EI II, Severinghaus JW. Effect of uneven pulmonary distribution of blood and gas on induction with inhalation anesthetics. *Anesthesiology* 1964; **25:** 620–6.
15. Elder JD Jr, Nagano SM, Eastwood DW, Harnagel D. Circulatory changes associated with thiopental anesthesia in man. *Anesthesiology* 1955; **16:** 394–400.
16. Sonntag H, Hellberg K, Schenk HD, Donath U, Regensburger D, Kettler D, Duchanova H, Larsen R. Effects of thiopental (Trapanal) on coronary blood flow and myocardial metabolism in man. *Acta Anaesthesiologica Scandinavica* 1975; **19:** 69–78.
17. Bahlman SH, Eger EI II, Halsey MJ, Stevens WC, Shakespeare TF, Smith NT, Cromwell TH, Fourcade H. The cardiovascular effects of halothane in man during spontaneous ventilation. *Anesthesiology* 1972; **36:** 494–502.
18. Bryce-Smith R, O'Brien HD. Fluothane: A non-explosive volatile anaesthetic agent. *British Medical Journal* 1956; **II:** 969–72.
19. Johnstone M. The human cardiovascular response to fluothane anaesthesia. *British Journal of Anaesthesia* 1956; **28:** 392–410.
20. Dundee JW, Barron DW, King R. The effect of methylation on the anaesthetic action of ethyl-methyl-propyl thiobarbiturate. *British Journal of Anaesthesia* 1960; **32:** 566–75.

Anaesthesia, 1986, Volume 41, pages 477–481

Alfentanil supplemented anaesthesia for short procedures

A double-blind study of alfentanil used with etomidate and enflurane for day cases

R. I. W. COLLIN, G. B. DRUMMOND AND A. A. SPENCE

Summary

Thirty-nine unpremedicated patients who presented for cystoscopy were given either alfentanil or saline in a random double-blind fashion immediately before anaesthesia with etomidate, nitrous oxide and enflurane. Alfentanil significantly reduced myoclonus associated with etomidate. During anaesthesia, patients who received alfentanil had smaller minute volumes, lower respiratory frequencies, and smaller increases in heart rate. The incidence of apnoea was not significantly increased. After operation, patients who received alfentanil were prescribed significantly more analgesia, possibly because of their reduced uptake of volatile anaesthetic agent. It is concluded that supplementation with alfentanil improves the quality of anaesthesia induced with etomidate.

Key words

Analgesies, narcotic; alfentanil.
Anaesthetics, intravenous; etomidate.

An anaesthetic technique for day case surgery should ideally use anaesthetic agents that are no longer active when the patient is discharged. Alfentanil appears to fulfil this criterion,[1] as does etomidate which, in addition, is an agent noted for its cardiovascular stability, lack of respiratory depression[2] and paucity of histamine-mediated anaphylactoid reactions.[3] Unfortunately, etomidate has the disadvantages of causing myoclonus, pain on injection, hiccup and cough.[2]

A number of clinical studies have used alfentanil to supplement anaesthesia with intermittent methohexitone or Althesin or etomidate, sometimes combined with nitrous oxide.[4–6] On some occasions, techniques based on etomidate were unsatisfactory because of excessive patient movement, and had to be abandoned to allow surgery to proceed. This happened so frequently in one study that the technique of combining etomidate, alfentanil and nitrous oxide was not pursued, and it was suggested that the addition of a volatile agent might be preferred.[5]

The present study was designed to test in a double-blind fashion, the influence of alfentanil given as a bolus on the quality of anaesthesia. This was assessed in four phases: induction, maintenance, short term recovery and long term recovery.

Methods

The study was approved by the local ethics committee. Thirty-nine patients about to undergo cystoscopy under general anaesthesia

---

R.I.W. Collin, MB, BS, Registrar, G.B. Drummond, MB, ChB, FFARCS, Senior Lecturer, A.A. Spence, MD, FFARCS, Professor, Anaesthetic Department, Royal Infirmary, Edinburgh EH3 9YW.

0003–2409/86/050477 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

gave written informed consent to participate. The age, weight, smoking habits and alcohol intake of the patients were noted and their exercise tolerance was graded.[7]

Before anaesthesia, a base-line score using the post box test[8] as modified by Patrick *et al.*[5] was obtained. The score was the time taken to post all sixteen blocks of various shapes into a posting box. No patient received premedication. All the anaesthetics were given by the same anaesthetist, who also assessed the patients. A cannula was inserted into a vein on the dorsum of the left hand. Control measurements of heart rate and arterial pressure were made using a Dinamap apparatus (No. 1846) with a printer. The patients were randomly allocated to receive an injection of either alfentanil 7 μg/kg or an equivalent volume of 0.9 percent sodium chloride on a double-blind basis. Sixty seconds later, anaesthesia was induced with 0.2 mg/kg etomidate intravenously over 10–15 seconds.

After induction, pain and myoclonus were graded as follows: pain on injecting etomidate: 0, none; 1, revealed by enquiry; 2, obvious by the patient grimacing or complaining; myoclonus, defined as rhythmical shaking of any part of the patient: 0, not present; 1, barely noticeable; 2, obvious; 3, patient's position on the table altered. Apnoea was defined as a respiratory pause of more than 20 seconds. The occurrence of hiccup and cough were recorded. In 29 of the patients, heart rate and arterial pressure, respiratory frequency and minute volume (Magtrak respirometer) were recorded at one minute intervals.

Anaesthesia was maintained with enflurane in 60 percent nitrous oxide in oxygen, using a circle system and CO_2 absorber; fresh gas flow rates were initially 6 then 3 litres/minute. The time from induction of anaesthesia to insertion of the cystoscope was noted and the response to instrumentation was graded as follows: 0, no response; 1, barely noticeable movement; 2, movement noticed by surgeon who was able to continue the procedure; 3, procedure delayed.

The time of cessation of administration of the anaesthetic was noted. In the recovery room, the patients were observed by nursing staff who were unaware of the nature of the preceding anaesthetic, and who recorded the times of recovery (opening eyes, protruding tongue and saying full name correctly.) Two hours after opening their eyes, the patients performed the postbox test again. The occurrence of nausea, vomiting, pain and the analgesics given were noted.

Before the code was broken, the overall quality of anaesthesia was assessed, and the anaesthetist attempted to predict from this whether the patient had received alfentanil or saline.

Statistical analysis was by Student's *t*-test for height, weight and control heart rate and arterial blood pressure measurements. For all other data, Fisher's exact test[9] or the Mann-Whitney U test[10] were used as appropriate. Statistical significance, where indicated, represents a probability value of 0.05 or less.

Results

Demography

There was no significant difference between the groups in respect of age, weight, height, sex distribution, smoking habits, alcohol intake and exercise tolerance. Since the patients' ages were not normally distributed, a non-parametric test was used to assess differences between the groups (Table 1). In addition, there were no statistical differences between the groups (height, weight and age) for the 29 patients from whom the cardiovascular and respiratory data were collected.

Induction characteristics (Table 2)

Alfentanil significantly reduced the incidence of myoclonus associated with etomidate administration ($p<0.05$); the probability in any particular patient was 0.7. Although mild pain appeared to be abolished by alfentanil, there was no statistical difference between the groups. There was a greater incidence of apnoea in the patients who received alfentanil (42 percent) compared with

Table 1. Patient demography, means (SD)

	n	Age (years)	Weight (kg)	Height (m)	Sex (M/F)	Smokers
Saline	20	45 (18)	72 (15)	1.67 (0.11)	12/8	9
Alfentanil	19	54 (13)	72 (10)	1.69 (0.07)	14/5	3

Table 2. Induction characteristics

		Number of subjects														
	n	Severity of myoclonus				Pain with etomidate			Apneoa	Hiccup	Cough	Response to instrumentation			
Grade		0	1	2	3	0	1	2				0	1	2	3
Saline	20	4	6	8	2	12	4	4	3	1	4	11	4	3	2
Alfentanil	19	9	7	2	1	16	0	3	8	0	4	13	5	0	1
p		<0.5				NS			NS	NS	NS	NS			

those who received saline (15 percent), but the difference was not significant. The incidence of cough and hiccup in both groups was similar.

The mean interval between induction of anaesthesia and the start of instrumentation was similar for both the alfentanil and saline groups. There was less response, although not significantly so, to instrumentation in those who received alfentanil.

Maintenance indices: cardiovascular and respiratory data

There was no significant difference between the groups in terms before induction of anaesthesia, of heart rate and mean arterial pressure. Compared with the control values, heart rate increased in both groups; it reached a maximum in the second to third minute after administration of alfentanil or saline, then steadily decreased. However, the heart rate in patients who received alfentanil remained consistently 8–14 beats/minute less than those who received saline (Fig. 1). Mean arterial blood pressure increased in both groups to a maximum of 120 mmHg at a similar time, then steadily decreased. In general, instrumentation was commenced after these maxima had been attained.

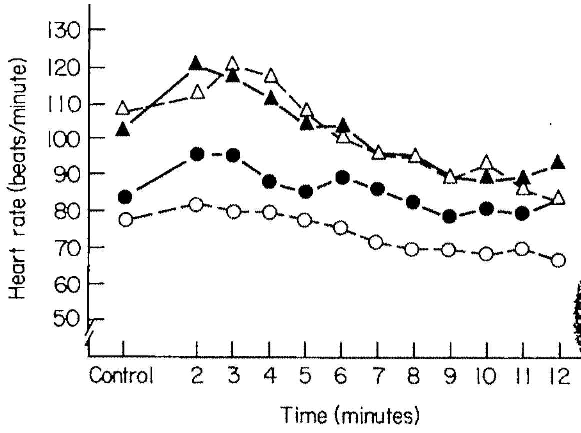
Minute volume and respiratory frequency were decreased in patients who received alfentanil. By the ninth minute, minute volumes were broadly similar in both groups, but the respiratory frequency in the alfentanil group was still substantially lower than in those who had received saline. (Fig. 2).

Short term recovery

The data from one patient were excluded from statistical analysis because the procedure lasted more than half an hour. The mean duration of general anaesthesia in both groups was 11 minutes. In patients who received alfentanil, the early recovery times were approximately one minute less than in the control group, but the difference was not significant (Table 3).

Long term recovery

The incidence of nausea, vomiting, administra-



• UNIVERSITY
LIBRARY

Fig. 1. Mean arterial pressure (top) and heart rate (bottom) for alfentanil and saline groups. ▲—▲, MAP saline; △—△, MAP alfentanil; ●—●, heart rate saline; ○—○, heart rate alfentanil.

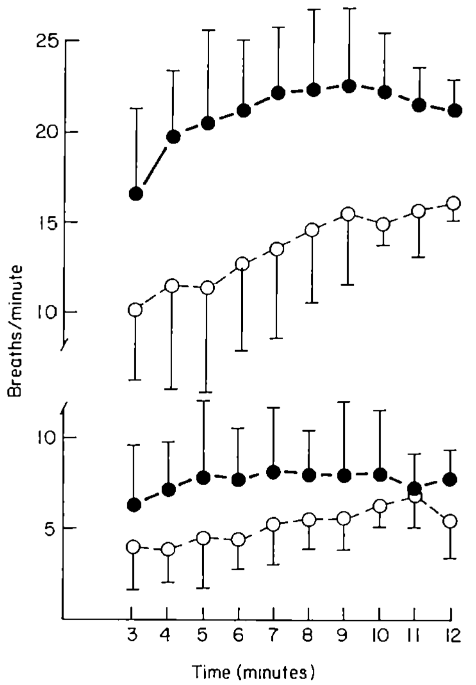


Fig. 2. Respiratory frequency (top) and minute volume (bottom) for alfentanil and saline groups. O—O, alfentanil; ●—●, saline.

tion of anti-emetics, and pain after operation was greater in the patients who received alfentanil. Four patients in the alfentanil group were prescribed analgesics, whereas no patient in the saline group was given an analgesic. ($p<0.05$, Table 4).

Post box scores

There was no significant difference between the groups either before or after the operation, nor was there any significant change in the performance of the test before or after operation in either group. (Table 4).

Assessment and prediction from overall quality of anaesthesia

Prediction by the anaesthetist of the drug administered (alfentanil or saline) was correct in 33 of the 39 cases (85 percent, $p<0.001$ by the Binomial theorem).

Discussion

The use of alfentanil compared with saline to supplement outpatient anaesthesia induced with etomidate and maintained with nitrous oxide and enflurane, was associated with a reduction in myoclonus. Heart rate, respiratory frequency and ventilation were reduced. The increased need for analgesia after the procedure may be related to the reduced uptake of volatile anaesthetic and hence less residual anaesthesia.

The maximum effect of alfentanil occurs within one minute of injection[1] and the sequence was designed to take maximum advantage of this. It might have been expected that pain on injection would be reduced. However, although mild pain was abolished, severe pain was unaffected. It was also expected that alfentanil, in common with other opioids, might have reduced the incidence of coughing, but this was not seen. Apnoea

Table 3. Short term recovery times, minutes (SD)

	Opening eyes	Showing tongue	Saying full name
Saline	5.3 (2.8)	5.6 (2.9)	6.1 (3.0)
Alfentanil	4.2 (2.2)	4.3 (2.4)	4.6 (2.4)
p	NS	NS	NS

Table 4. Long term recovery

	Saline	Alfentanil	p
Nausea	2	6	NS
Vomiting	2	5	NS
Pain	5	9	NS
Receiving anti-emetics	0	2	NS
Receiving analgesics	0	4	<0.5
Postbox scores (SD)			
Before operation	29 (6)	29 (5)	NS
After operation	27 (5)	27 (5)	NS

occurred in both groups, but in no case was it considered necessary to assist ventilation. It was never necessary to abandon the anaesthetic sequence in either group.

When considering the increased incidence of pain after the anaesthetic in the alfentanil group, it should be noted that some of this included headache persisting from before the anaesthetic and we did not collect data to compare the incidences between the groups for such complaints prior to giving the anaesthetic.

If a given time span is given to perform the post-box test, subjects learn to post the easy shapes. To avoid this problem we asked patients to post all the shapes. We also asked that patients use only their dominant hand. Patients undertook only two trials with the postbox as we were seeking to compare the long term recovery between the groups, not establish the precise time at which the patients could be considered to have fully recovered.

Other workers have also studied methods of anaesthesia with etomidate in comparison or combination with alfentanil,[4–6] halothane[6] and thiopentone.[11] Some of these stated that it was necessary to abandon the technique so that operation could take place.[4,5] We are not aware of any other work where alfentanil was given in a double-blind manner, followed by induction with etomidate and maintenance with a volatile agent and nitrous oxide. The addition of a volatile agent appears to confer a greater reliability on techniques based on etomidate.

We confirmed the findings of Antonios, Inglis and Lees[6] in that the incidence of myoclonus was significantly reduced when pretreating with alfentanil. We also found that the heart rate was reduced in the alfentanil group. The rate–pressure product was reduced and, consequently, myocardial oxygen requirement was probably less. This is an advantage when dealing with patients who may have ischaemic heart disease.

We found the use of alfentanil and etomidate for induction of anaesthesia followed by nitrous oxide and enflurane highly satisfactory when the requirements are swift induction of anaesthesia in patients and fast, safe recovery.

Acknowledgments

We would like to thank Janssen Pharmaceuticals Ltd for providing the measuring apparatus. The cooperation and assistance of our surgical colleagues and the theatre and recovery staff was invaluable.

References

1. Cookson RF, Niemegeers CJE, Vanden Bussche G. The development of alfentanil. *British Journal of Anaesthesia* 1983; **55:** 147S–55S.
2. Nimmo WS, Miller M. Pharmacology of etomidate. In: Brown BR Jr., ed. *New pharmacologic vistas in anesthesia*. F.A. Davis, 1983.
3. Watkins J. Etomidate: an 'immunologically safe' anaesthetic agent. *Anaesthesia* 1983; **38** supplement: 34–8.
4. Kay B. Cohen AT. Intravenous anaesthesia for minor surgery. A comparison of etomidate or Althesin with fentanyl and alfentanil. *British Journal of Anaesthesia* 1983; **55:** 165S–7S.
5. Patrick M, Eagar BM, Toft DF, Sebel PS. Alfentanil-supplemented anaesthesia for short procedures. A double-blind comparison with fentanyl. *British Journal of Anaesthesia* 1984; **56:** 861–5.
6. Antonios WRA, Inglis MD, Lees NW. Alfentanil in minor gynaecological surgery: use with etomidate and a comparison with halothane. *Anaesthesia* 1984; **39:** 812–5.
7. Lunn JN, Muir JR. Heart disease. In: Vickers MD, ed. *Medicine for anaesthetists*. Oxford: Blackwell, 1977: 3.
8. Craig J, Cooper GM, Sear JW. Recovery from day-case anaesthesia. Comparison between methohexitone, Althesin and etomidate. *British Journal of Anaesthesia* 1982; **54:** 447–50.
9. Maxwell AE. *Analysing qualitative data*. London: Chapman and Hall, 1961 (paperback 1975) 23–6.
10. Moses LE, Emerson JD, Hosseini H. Statistics in practice; analysing data from ordered categories. *The New England Journal of Medicine* 1984; **311:** 442–8.
11. Lowe SS. The prevention of etomidate-induced myoclonus. *Anaesthesia* 1984; **39:** 70–1.

Anaesthesia, 1986, Volume 41, pages 482–485

Sensitivity to propofol in the elderly

J. W. DUNDEE, FRANCES P. ROBINSON, J. S. C. McCOLLUM
AND C. C. PATTERSON

Summary

Two studies were carried out on 609 fit, unpremedicated patients to assess the influence of patient age on the response to the rapidly-acting hindered phenol, propofol, which is being evaluated for induction of anaesthesia. In the first study, 1.25 mg/kg was injected over 20 seconds followed by 10-mg increments every 15 seconds until loss of verbal contact. This showed a great individual variation in response to the drug. A reduction in the 'induction' dose was found in elderly patients, which became marked around 60 years. In the second (340), doses ranging from 1.5–3.0 mg/kg in patients under 60 years and 1.25–2.25 mg/kg in those over 60 years were injected as a bolus over 20 seconds. Doses of 2.25–2.5 mg/kg were required to induce anaesthesia in patients under 60 years, whilst 1.5–1.75 mg/kg was adequate in those over 60 years. Side effects were more marked with the rapid injection and doses in excess of 1.75 mg/kg caused significant hypotension and apnoea in the elderly. These studies reveal marked sensitivity to propofol in the elderly with respect to both induction dose and acute toxicity.

Key words

Anaesthetics, intravenous; propofol.

One is becoming increasingly aware of the decreased tolerance to drugs in elderly patients; this could be a particularly important problem with intravenous anaesthetics where an immediate 'bolus' effect occurs. Elderly patients require relatively small doses of thiopentone,[1,2] an effect attributable to altered initial volume of distribution.[2] The onset time with midazolam is shorter in the elderly,[3] an effect likewise attributable to altered pharmacokinetics.[4]

This paper reports two studies on the influence of age on response to the hindered phenol, propofol, a new, rapidly-acting intravenous anaesthetic.[5] The first study, based on a method described for thiopentone,[1] is only applicable to drugs which, in adequate doses, induce anaesthesia in one arm–brain circulation time and we have shown that this applies to propofol.[6] In the second study, the effects of doses ranging from 1.5–3.0 mg/kg in patients under 60 years and 1.25–2.25 mg/kg in older patients were studied. Both studies were approved by the regional medical ethical committee.

Method

All studies were carried out in fit, unpremedicated adults who had agreed to participate in the trial

---

J.W. Dundee, MD, PhD, FRCP, FFARCS, Professor, Frances P. Robinson, MB, FFARCS, Research Fellow, J.S.C. McCollum, MB, FFARCS, Lecturer, Department of Anaesthetics, C.C. Patterson, MSc, Lecturer, Department of Medical Statistics, The Queen's University of Belfast, Northern Ireland.

0003–2409/86/050482 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

and who were scheduled for intravenous induction of anaesthesia. Grossly obese and pregnant patients were excluded from the trial and patients' weights ranged from 40–80 kg. All injections were given into large antecubital or forearm veins. Vital signs were recorded before and at one-minute intervals following injection, until administration of other drugs or commencement of the operation.

Dose finding study

An initial dose of 1.25 mg/kg was given over 20 seconds with increments of 10mg every 15 seconds until loss of verbal contact with the patient occurred. This was taken as the induction dose and anaesthesia continued with further propofol or other drugs as necessary. The study ended when there was a minimum of 30 patients in each 10-year age band from 20 to 80 years and 27 in the 16–19 year age group.

Scanning of the results showed a wide variability of readings, especially in the younger age group and in the subsequent statistical analysis using log transformed data. Multiple regression analysis was used to fit polynomial terms in age to the dose requirements (mg/kg) and a separate analysis was carried out for males and females.

Bolus doses

Patients under 60 years were given, in random order, bolus doses ranging from 1.5–3.0 mg/kg, again injected over 20 seconds. In older patients, the doses ranged from 1.25–2.25 mg/kg. There were 30 patients in each group, except for the lowest and highest doses in the elderly patients, where the number was 20. In addition to noting when consciousness was lost, rapid lightening of anaesthesia, (making difficulties with subsequent maintenance) was noted, as was the frequency of spontaneous excitatory and respiratory side effects. The actual duration of apnoea was noted up to 61 seconds, after which ventilation was assisted.

Results

Anaesthesia was smooth in most instances, with the very rare occurrence of troublesome spontaneous movement or respiratory upset. Figure 1 shows an obvious reduction in dosage in both sexes in patients over 60 years of age. The variation in dosage in also less in the elderly patients. The lines in Fig. 1 are calculated at the mean weight for each group and the slight difference between males and females is not clinically significant. The statistically derived formulae for the lines of best fit are:

Men, $\log_e \text{dose} = 1.082 - 0.0054\ (\text{age}-45) - 0.00014\ (\text{age}-45)^2 - 0.0055 \times \text{weight}$

Women, $\log_e \text{dose} = 1.073 - 0.0031\ (\text{age}-45) - 0.00015\ (\text{age}-45)^2 - 0.0069 \times \text{weight}$

Table 1 gives the mean doses in patients under and over 60 years. With both series there is a highly significant ($p < 0.001$) difference between the requirements in the two age groups. With this technique of 'induction', the frequency of side effects attributable to propofol was low and with the reduced dosage in the elderly, no obvious age-related cardiovascular or respiratory depression was recorded. Table 2 summarises the findings of the bolus study. The lowest (1.25 mg/kg) dose was abandoned after 20 administrations because of

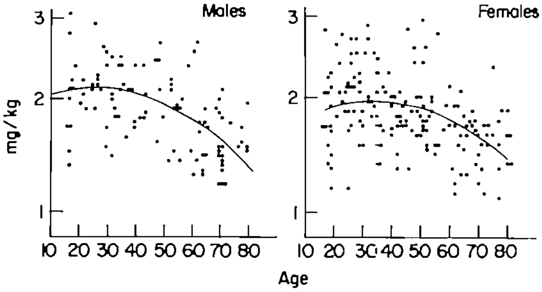


Fig. 1. Plot of 'induction' dose requirements of propofol versus age for each individual patient, together with line of best fit calculated by multiple regression analysis.

Table 1. Mean induction dose of propofol in patients under and over 60 years

	Under 60 years			Over 60 years		
	n	mg/kg	(SD)	*n*	mg/kg	(SD)
Males	69	2.08	(0.37)	37	1.66	(0.33)
Females	118	1.97	(0.39)	45	1.63	(0.25)

extremely light anaesthesia in six patients. The highest dose in the elderly was stopped at 20 administrations because of an excessive incidence of hypotension and apnoea.

Doses of 2.25–2.50 mg/kg are required to induce anaesthesia in the patients under 60 years while 1.50–1.75 mg/kg is adequate in the older patients. Prolonged apnoea becomes a problem with doses greater than 2.5 mg/kg in young patients and with doses of 2.0 mg/kg and over in the elderly. The most important difference between the two series is the higher incidence of hypotension and apnoea when a bolus is injected over 20 seconds, compared with virtually complete absence of acute toxicity with the slower injection.

Discussion

The two studies show marked sensitivity to the drug in elderly patients, both with respect to dosage and acute toxic effects. The latter can be minimised by a slow injection technique, such as that used in the dose-finding study. When given slowly and in small dosage, propofol proved to be a satisfactory drug in elderly patients.

The 'induction' dose of propofol, as estimated in this study, differs slightly from the requirements when the drug is used in clinical practice. These differences will apply in all age groups except that a slow circulation time could result in some overestimate of dosage in the elderly. The negative coefficients for weight in the formulae indicate that the administration of propofol on a weight basis overcorrects. With thiopentone, the weight-related calculated dose is reduced in obese patients and it has been suggested the dosage should be related to lean body mass.[7] However, this is clinically not practical.

No pharmacokinetic studies were carried out in these patients as it was our intention to look at the degree rather than the cause of changes in dosage requirements.

Acknowledgment

Thanks are due to Imperial Chemical Industries plc for supplies of propofol and interest in the study.

References

1. DUNDEE JW, HASSARD TH, MCGOWAN WAW, HENSHAW J. The 'induction' dose of thiopentone. A method of study and preliminary illustrative results. *Anaesthesia* 1982; **37**: 1176–84.

Table 2. Frequency (%) of adequate induction of anaesthesia, hypotension and apnoea with varying single bolus doses of propofol in two age groups ($n = 30$, except $^*n = 20$)

Dose (mg/kg)	Under 60 years					Over 60 years				
	Anaesthesia induced	Systolic BP decrease (mmHg)		Apnoea (seconds)		Anaesthesia induced	Systolic BP decrease (mmHg)		Apnoea (seconds)	
		21–40	41+	31–60	61+		21–40	41+	31–60	61+
1.25						*100 (30)	35	15	10	15
1.50	53 (13)	20	3	17	3	97 (3)	27	13	23	7
1.75	83 (17)	40	0	30	7	100 (0)	50	13	40	7
2.00	87 (10)	23	0	20	10	97 (0)	40	20	53	20
2.25	97 (0)	50	0	30	13	*100 (0)	35	45	30	25
2.50	100 (3)	33	13	64	13					
2.75	100 (0)	40	3	20	40					
3.00	100 (0)	33	10	23	43					

Figures in brackets indicate rapid lightening of anaesthesia

2. Homer TD, Stanski DR. The effects of increasing age on thiopental disposition and anaesthetic requirements. *Anesthesiology* 1985; **62:** 714–24.
3. Dundee JW, Halliday NJ, Loughran PG, Harper KW. The influence of age on the onset of anaesthesia with midazolam. *Anaesthesia* 1985; **40:** 441–3.
4. Halliday NJ, Dundee JW, Loughran PG, Harper KW. Age and plasma proteins influence the action of midazolam. *Anesthesiology* 1984; **61:** A357.
5. Glen JB, Hunter SC. Pharmacology of an emulsion preparation of ICI 35 868. *British Journal of Anaesthesia* 1984; **56:** 617–26.
6. Robinson FP, Dundee JW, Halliday NJ. Effects of age on 'induction dose' of propofol. *British Journal of Anaesthesia* 1985; **57:** 349P.
7. Wulfsohn NL, Joshi CW. Thiopentone dosage based on lean body mass. *British Journal of Anaesthesia* 1969; **41:** 516–21.

Anaesthesia, 1986, Volume 41, pages 486–492

Premedication with cimetidine and metoclopramide

Effect on the risk factors of acid aspiration

S. K. PANDIT, S. P. KOTHARY, UMA A. PANDIT AND R. K. MIRAKHUR

Summary

A randomised, double-blind, placebo-controlled parallel study was conducted in adult females to evaluate the efficacy and safety of a combination of cimetidine 300 mg orally and metoclopramide 10 or 20 mg intravenously in reducing pre-operative residual gastric volume and raising gastric pH. The effect of pre-operative metoclopramide on postoperative nausea and vomiting was also investigated. Oral cimetidine was given approximately 2–2.5 hours before, and intravenous metoclopramide either 15 or 30 minutes prior to induction of anaesthesia. The study showed that placebo-treated patients undergoing outpatient operations have an increased risk of acid aspiration because of high residual gastric volume and low pH and increased risk of serious pulmonary injury should acid aspiration occur. Metoclopramide 10 or 20 mg intravenously prior to induction of anaesthesia was effective in reducing the residual gastric volume significantly, but not in raising pH. The combination of cimetidine and metoclopramide, as well as cimetidine alone, reduced the risk factors of acid aspiration by raising gastric pH and reducing residual volume. No anti-emetic effect of metoclopramide was observed. Higher doses of metoclopramide (20 mg) produced significant side effects (flushing, dizziness, extrapyramidal side effects), but were only marginally more effective than 10 mg doses in reducing residual gastric volume.

Key words

Gastrointestinal tract; stomach, pH.
Histamine; H_2-receptor antagonist, cimetidine.
Pharmacology; metoclopramide.

Much has been written about the risk of acid aspiration during anaesthesia, and various methods have been suggested to reduce this hazard. Yet the aspiration of stomach contents still remains a major cause of anaesthetic mortality and morbidity.[1] Thus, continued research in this area is indicated.[2] The introduction of cimetidine (an H_2-receptor blocker) was undoubtedly a breakthrough in approaching the problem of acid aspiration during anaes-

---

S.K. Pandit, MD, Professor of Anesthesiology, S.P. Kothary, MD, Senior Research Associate, Uma A. Pandit, MD, Assistant Professor, University of Michigan Hospital, 1405 E. Ann Street, Ann Arbor, Michigan 48109, R.K. Mirakhur, MD, Consultant Anaesthetist, Royal Victoria Hospital, Northern Ireland.

Correspondence should be addressed to: Sujit K. Pandit please.

This work was supported partly by a grant from A.H. Robins Company. Some of the results were presented at the Annual Meeting of the International Anesthesia Research Society, Reno, Nevada, March 10–14, 1984.

0003–2409/86/050486 + 07 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

thesia.[3-10] Cimetidine, given at least 60–120 minutes before the induction of anaesthesia (either orally, intramuscularly or intravenously, predictably raises the gastric pH to a safer level.[7-10] However, it is claimed that a single dose of cimetidine does not always reduce residual gastric volume.[8,10] Undoubtedly, intragastric pH is a more important factor than volume in determining the consequences of aspiration,[11] but high residual gastric volume and consequent high intragastric pressure certainly can precipitate or facilitate regurgitation and aspiration.

Metoclopramide, a dopamine antagonist and anti-emetic, accelerates gastric emptying by increasing motility of the gastrointestinal tract and increasing lower oesophageal sphincter pressure.[12,13] At present, metoclopramide is commonly used in radiological procedures of the gastrointestinal tract,[14] as an anti-emetic after cancer chemotherapy,[15] and as a gastric prokinetic agent in diabetic gastroparesis.[16]

Our study examines whether a combination of cimetidine and metoclopramide would be more effective than either drug alone in reducing the accepted risk factors of acid aspiration, without causing additional side effects.

Methods

The study consisted of two separate and independent phases.

Phase 1

Eighty adult female patients (ASA Class 1 or 2) scheduled for outpatient laparoscopic examination or laparoscopic tubal cauterisation were randomly divided into four test groups. The institutional ethics committee approved the study and each patient gave written informed consent. All patients fasted for at least 10 hours before operation and no premedication other than the study drugs was given. The study medications were dispensed in a randomised double-blind fashion. The staff of the hospital pharmacy blinded the medication in identical containers (capsules and vials) and randomisation was done by a computer. Each patient received one capsule (placebo or cimetidine 300 mg) administered orally approximately 2 hours before operation, and an intravenous agent (placebo or metoclopramide 10 mg) approximately 15 minutes prior to induction of anaesthesia. The intravenous agents (2 ml) were injected over a period of 60 seconds. Lactose was used as placebo for oral medication and 0.9 percent sodium chloride was used as the placebo for intravenous medication. Group 1 patients received placebo orally and placebo intravenously, group 2 patients received placebo orally and metoclopramide intravenously, group 3 patients received cimetidine orally and metoclopramide intravenously, and group 4 patients received cimetidine orally and placebo intravenously (Table 1).

Anaesthetic management in all cases was standardised; pretreatment with tubocurarine (3 mg), induction with thiopentone (4–5 mg/kg), suxamethonium (1.5–2.0 mg/kg) tracheal intubation; anaesthesia was maintained with nitrous oxide, oxygen, a volatile anaesthetic agent (usually isoflurane), fentanyl (1–2 μg/kg), suxamethonium infusion and controlled ventilation. Immediately following tracheal intubation, a Salem sump gastric tube (16 or 18 SWG) was passed via the mouth; position was confirmed by auscultation of injected air and as much gastric juice as possible was aspirated after repeated changes in the position of the stomach tube and of the patient. The aspiration of the stomach content was done over a period of 20–30 minutes.

Table 1. Phase 1: Demography (mean, SEM)

Drug group	n	Age (years)	Height (inches)	Weight (lb)
1 Oral placebo + intravenous placebo	20	30.67 (1.44)	63.62 (0.62)	142.19 (7.09)
2 Oral placebo + intravenous metoclopramide 10 mg	20	27.95 (0.98)	64.67 (0.73)	136.76 (5.04)
3 Oral cimetidine 300 mg + intravenous metoclopramide 10 mg	20	32.60 (1.20)	63.95 (0.54)	136.50 (8.37)
4 Oral cimetidine 300 mg + intravenous placebo	20	32.75 (1.80)	64.75 (0.63)	130.85 (4.47)
		p = 0.06	p = 0.52	p = 0.67

Table 2. Phase 2: Demography (mean, SEM)

Drug group	n	Age (years)	Height (inches)	Weight (lb)
1 Oral cimetidine 300 mg + intravenous metoclopramide 10 mg	15	29.80 (1.27)	65.33 (0.65)	144.20 (6.42)
2 Oral cimetidine 300 mg + intravenous metoclopramide 20 mg	19	30.32 (1.28)	64.68 (0.60)	142.37 (7.08)
3 Oral cimetidine 300 mg + intravenous placebo	19	28.32 (1.06)	65.21 (0.84)	142.79 (5.75)
		$p = 0.46$	$p = 0.79$	$p = 0.98$

The pH of the collected juice was measured using a Corning pH meter and volume was measured accurately by syringe.

The incidence of pre-operative side effects such as dizziness or sedation, and postoperative side effects such as nausea, vomiting or drowsiness, were recorded following specific interrogation regarding presence or absence of the side effects.

Phase 2

An additional 53 adult female patients (ASA Class 1 or 2) scheduled for the same operation in the same operating room were studied after all the cases in Phase 1 were completed. Phase 2 study protocol was exactly the same as in Phase 1, except that there were three study groups and all patients received cimetidine 300 mg orally approximately 160 minutes beforehand, followed by either metoclopramide 10 mg or 20 mg or a placebo given 30 minutes before induction of anaesthesia rather than 15 minutes before, as was done in Phase 1 (Table 2). The study in Phase 2 was terminated before all the designated cases were completed because of the necessity of writing an abstract by a given deadline; hence, we have groups of unequal size.

Statistical analysis

Demographic data, time intervals after medications, residual gastric volumes and pH values obtained from each group were compared between groups in each Phase by the ANOVA one-way analysis of variance technique to test the null hypothesis. In the case of an overall significance, pairwise multiple comparisons were performed to find which groups accounted for that significance. The side effects (nausea, vomiting, dizziness, etc.) which occurred in each group were compared with those in other groups using the Chi squared statistic. A value of $p < 0.05$ was considered significant.

Results

Tables 1 and 2 show the demographic variables in Phases 1 and 2 respectively. There was no statistical difference between the groups studied during each phase. The actual time interval between the oral premedication and gastric suctioning and also between the intravenous premedication and gastric suctioning is shown in Table 3 (Phase 1) and Table 4 (Phase 2). As planned, the oral medication in Phase 1 was given

Table 3. Phase 1: actual time intervals (mean, SEM)

Drug group	Time interval between oral medication and gastric suction (minutes)	Time interval between intravenous medication and gastric suction (minutes)
1 Oral placebo + intravenous placebo	132.38 (8.77)	19.05 (1.81)
2 Oral placebo + intravenous metoclopramide 10 mg	142.86 (8.97)	17.62 (1.45)
3 Oral cimetidine 300 mg + intravenous metoclopramide 10 mg	149.75 (11.86)	18.25 (1.37)
4 Oral cimetidine 300 mg + intravenous placebo I.V.	137.00 (9.89)	18.00 (1.56)
	$p = 0.63$	$p = 0.93$

Table 4. Phase 2: actual time intervals (mean, SEM)

Drug group	Time interval between oral medication and gastric suction (minutes)	Time interval between I.V. medication and gastric suction (minutes)
1 Oral cimetidine 300 mg	152.00	32.33
+ intravenous metoclopramide 10 mg	(10.81)	(1.45)
2 Oral cimetidine 300 mg	160.79	34.21
+ intravenous metoclopramide 20 mg	(9.02)	(1.88)
3 Oral cimetidine 300 mg	161.32	35.79
+ intravenous placebo	(8.87)	(1.88)
	$p = 0.76$	$p = 0.42$

approximately 2–2.5 hours prior to the gastric suctioning and intravenous medication was administered approximately 15–20 minutes beforehand. In Phase 2, these were given approximately 2–2.5 hours and 30–35 minutes, respectively, prior to gastric suctioning. There was no statistical difference between the groups in this respect.

Table 5 shows the pH values (mean, SEM) and residual gastric volume (mean, SEM) in Phase 1 cases. When no active agent was given (group 1, placebo and placebo), the mean pH of the gastric juice was 2.03 (SEM 0.25) and the average gastric volume was 45.48 (SEM 5.73) ml. In group 2 (placebo and metoclopramide 10 mg), the average pH was still low (2.28, SEM 0.33), but the residual volume (24.10, SEM 3.4 ml) was significantly lower ($p < 0.001$) compared to group 1. Group 3 (cimetidine and metoclopramide) and group 4 (cimetidine and placebo) both had high pH (5.30, SEM 0.46 and 5.45, SEM 0.46, respectively), and both groups also had low residual volumes (17.65, SEM 3.07 and 17.90, SEM 3.0 ml, respectively). The pH values in groups 3 and 4 were significantly ($p < 0.001$) higher than both group 1 (placebo and placebo) and group 2 (placebo and metoclopramide). There was no significant difference between group 3 and 4 with respect to pH levels. Residual volumes in groups 3 and 4 were also significantly reduced ($p < 0.001$) compared to group 1 but not from group 2, group 3 and group 4 revealed no significant difference in volume aspirated.

Table 5. Phase 1: pH and volume of gastric juice (mean, SEM)

Drug group	pH of gastric juice	Residual volume (ml)
1 Oral placebo	2.03	45.48
+ intravenous placebo	(0.25)	(5.73)
2 Oral placebo	2.28	24.10*
+ intravenous metoclopramide 10 mg	(0.33)	(3.42)
3 Oral cimetidine 300 mg	5.30†*	17.65*
+ intravenous metoclopramide 10 mg	(0.46)	(3.07)
4 Oral cimetidine 300 mg	5.45†*	17.90*
+ intravenous placebo	(0.46)	(3.00)
	$p = 0.001$	$p = 0.001$

*$p < 0.001$ compared to group 1.
†$p < 0.001$ compared to group 2.

Table 6 shows the mean pH and residual volume in the three groups in Phase 2. The mean pH was high in all the three groups (well over 5), and with no statistical difference between the groups. The residual volumes in all the three groups were low and ANOVA analysis demonstrated no difference between the groups. No patient showed any clinical sign of aspiration either in Phase 1 or in Phase 2.

The only side effect encountered in Phase 1 (Table 7) was nausea and vomiting in a few cases in the postoperative period. Regardless of whether the patients received metoclopramide or not, the frequency of nausea and vomiting was very similar in all groups, with one exception. There was a statistical difference ($p < 0.05$) between group 2 and group 4 favouring placebo over metoclopramide. Therapy for nausea and vomit-

Table 6. Phase 2: pH and volume of gastric juice (mean, SEM)

Drug group	pH of gastric juice	Residual volume (ml)
1 Oral cimetidine 300 mg + intravenous metoclopramide 10 mg	5.36 (0.52)	16.73 (3.56)
2 Oral cimetidine 300 mg + intravenous metoclopramide 20 mg	5.81 (0.44)	14.79 (3.71)
3 Oral cimetidine 300 mg + intravenous placebo	5.60 (0.45)	23.95 (2.49)
	$p = 0.81$	$p = 0.11$

Table 7. Phase 1: side effects

Drug group	Nausea only	Nausea and vomiting	Therapy required	No side effects
1 Oral placebo + intravenous placebo	2/20	2/20	0/4	17/20
2 Oral placebo + intravenous metoclopramide 10 mg	0/20*	4/20*	1/4	17/20
3 Oral cimetidine 300 mg + intravenous metoclopramide 10 mg	2/20	2/20	0/4	16/20
4 Oral cimetidine 300 mg + intravenous placebo	5/20*	2/20*	1/7	13/20

*Chi squared statistics for group 2 versus group 4 = $p < 0.05$.

in was instituted when the signs and symptoms occurred more than twice.

In Phase 2 (Table 8), the frequency of nausea and vomiting in the three groups appeared very similar, although there was a statistical difference ($p < 0.05$) between group 2 and group 3, this time favouring metoclopramide over a placebo. Six patients out of 19 in Phase 2/group 2 (metoclopramide 20 mg) complained of transient flushing and dizziness soon after the intravenous medication, and one patient had extrapyramidal side effects (tonic contractions of ocular and facial muscles) which was treated promptly with diphenhydramine 25mg intravenously. One patient in group 1 (metoclopramide 10 mg) also complained of transient dizziness after the medication.

There was no difference between the groups in either Phase 1 or Phase 2 in the duration of recovery room stay or time to discharge.

Discussion

The incidence of morbidity and mortality from acid aspiration during elective operation is not known. However, the risk factors (low gastric pH, high residual volume and increased intragasric pressure) have been identified. Thus, in clinical practice, it is prudent to try to reduce these risk factors as much as possible, especially in patients who are known to be at higher risk of regurgitation (e.g. obese patients, anticipated difficult intubation, high anxiety). The patients who received no active treatment (Phase 1, group 1, placebo and placebo) had consistently low pH

Table 8. Phase 2: side effects

Drug group	Nausea only	Nausea and vomiting	Therapy required	Flushing and dizziness	Extra-pyramidal side effects	No side effects
1 Oral cimetidine 300 mg + intravenous metoclopramide 10 mg	4/15	2/15	3/6	1/15	0/15	8/15
2 Oral cimetidine 300 mg + intravenous metoclopramide 20 mg	3/19	1/19*	2/4*	6/19	1/19	8/19
3 Oral cimetidine 300 mg + intravenous placebo	3/19	5/19*	4/8*	0/19	0/19	11/19

*Chi squared statistics for group 2 versus group 3 = $p < 0.05$.

and high gastric volume. The results found in this control group are comparable to those reported in other published work.[3–11] It has been suggested that patients scheduled for outpatient operation have higher residual gastric volume and lower pH compared to inpatients,[17] and thus presumably are at higher risk for pulmonary injury if acid aspiration occurs, although these data have not been verified in other studies. By current standards, the untreated patients in our study are at higher risk of acid aspiration compared to the treated group.

We confirmed the results of Wymer and Cohen,[18] who found that metoclopramide 10 mg given intravenously 15 minutes before operation, significantly reduced the gastric fluid volume but did not alter the pH. We also confirmed the results obtained by Capan *et al.*[19] that there was no significant difference in the intragastric pH and volume between the groups who received cimetidine alone and those who received cimetidine and metoclopramide (10 mg). Was this because of an insufficient dose of metoclopramide (10 mg) or because sufficient time (more than 15 minutes) was not allowed after the administration of the medication? In Phase 2, we addressed these two issues and increased the dose of metoclopramide to 20 mg and allowed at least 30 minutes after the metoclopramide. ANOVA analysis indicated that residual gastric volume was marginally better in patients who had received metoclopramide 20 mg (compared to placebo), but not significantly so; however, the metoclopramide 20 mg group had an unacceptably high frequency of side effects, especially dizziness. There was no difference in results between metoclopramide given 15 minutes versus 30 minutes prior to induction of anaesthesia (Phase 1 versus Phase 2). We have not analysed our data on the basis of popularly accepted high risk factors viz. pH less than 2.5 plus gastric volume more than 25 ml, because we believe these numbers have not been scientifically corroborated as yet. Manchikanti *et al.*[20] recently concluded that oral administration of cimetidine and metoclopramide in combination may reduce the risk of acid aspiration syndrome because the combination modifies accepted risk factors. However, careful analysis of their results clearly showed that cimetidine alone, given at bedtime and mornings, worked just as well as the combination of cimetidine and metoclopramide to reduce the accepted risks (pH 2.5 and gastric volume 25 ml). We found similar results with a single dose of cimetidine given in the morning.

The anti-emetic effect of metoclopramide is not evident. This may be due to the short half life of metoclopramide,[12,21] and when given pre-operatively (especially intravenously), the anti-emetic effect may not extend to the postoperative period. Several other investigators[22–24] also showed that pre-operative metoclopramide is not an effective postoperative anti-emetic.

Thus, we conclude that unmedicated adult female patients scheduled for outpatient laparoscopic procedure have a large residual gastric volume and low pH. A single dose of cimetidine given orally at least 2 hours before induction of anaesthesia should significantly reduce the accepted risk factors (pH and volume) for acid aspiration and reduce the chance of significant pulmonary injury should acid aspiration occur. A pre-operative combination of cimetidine orally and metoclopramide intravenously also reduces the risk factors, but not any more than cimetidine alone. However, the combination may have an advantage because metoclopramide is known[25] to increase lower oesophageal sphincter tone and thus should prevent regurgitation.

References

1. Lunn JN, Mushin WW. *Mortality associated with anaesthesia*. London: The Nuffield Provincial Hospital Trust, 1982.
2. Coombs DW. Aspiration pneumonia prophylaxis. (Editorial). *Anesthesia and Analgesia* 1983; **62:** 1055–8.
3. Coombs DW, Hooper D, Colton T. Pre-anesthetic cimetidine alteration of gastric fluid volume and pH. *Anesthesia and Analgesia* 1979; **58:** 183–8.
4. Husemeyer RP, Davenport HT, Rajasekaran T. Cimetidine as a single dose for prophylaxis against Mendelson's syndrome. *Anaesthesia* 1978; **33:** 775–8.
5. Stoelting RK. Gastric fluid pH in patients receiving cimetidine. *Anesthesia and Analgesia* 1978; **57:** 675–7.
6. Kirkegaard P, Sorensen O, Kirkegaard P. Cimetidine in the prevention of acid aspiration during anesthesia. *Acta Anaesthesiologica Scandinavica* 1980; **24:** 58–60.
7. Weber L, Hirshman CA. Cimetidine for prophylaxis of aspiration pneumonitis: comparison of intramuscular and oral dosage schedules. *Anesthesia and Analgesia* 1979; **58:** 426–7.
8. Detmer MD, Pandit SK, Cohen PJ. Prophylactic single-dose oral antacid therapy in the preoperative period—comparison of cimetidine and Maalox. *Anesthesiology* 1979; **51:** 270–3.
9. Coombs DW, Hooper DW. Cimetidine as a

prophylactic against acid aspiration at tracheal extubation. *Canadian Anaesthetists' Society Journal* 1981; **28:** 33–8.

10. Williams JG. H_2 receptor antagonists and anaesthesia. *Canadian Anaesthetists' Society Journal* 1983; **30:** 264–9.
11. James CF, Modell JH, Gibbs CP, Kuck EJ, Ruiz BC. Pulmonary aspiration—effects of volume and pH in the rat. *Anesthesia and Analgesia* 1984; **63:** 665–8.
12. Albibi R, McCallum RW. Metoclopramide: clinical pharmacology and clinical application. *Annals of Internal Medicine* 1983; **98:** 86–95.
13. Schulze-Delrieu K. Metoclopramide. *New England Journal of Medicine* 1981; **305:** 28–33.
14. James WB, Hume R. Action of metoclopramide on gastric emptying and small bowel transit time. *Gut* 1968; **9:** 203–5.
15. Gralla RJ, Itri LM, Pisko SE, Squillante AE, Kelsen DP, Braun DW, Jr., Bordin LA, Braun TJ, Young CW. Antiemetic efficacy of high-dose metoclopramide: randomized trials with placebo and prochlorperazine in patients with chemotherapy-induced nausea and vomiting. *New England Journal of Medicine* 1981; **305:** 905–9.
16. Campbell IW, Heading RC, Tothill P, Buist TAS, Ewing DJ, Clarke BF. Gastric emptying in diabetic autonomic neuropathy. *Gut* 1977; **18:** 462–7.
17. Ong BY, Palahniuk RJ, Cumming M. Gastric volume and pH in out-patients. *Canadian Anaesthetists' Society Journal* 1978; **25:** 36–9.
18. Wymer J, Cohen SE. Gastric volume in early pregnancy: effect of metoclopramide. *Anesthesiology* 1982; **57:** 209–12.
19. Capan LM, Rosenberg AD, Carni A, Patel KP, Sheth R, Kitain E, Turndorf H. Effect of cimetidine–metoclopramide combination on gastric fluid volume and acidity. *Anesthesiology* 1983; **59:** A402.
20. Manchikanti L, Marrero TC, Roush JR. Preanesthetic cimetidine and metoclopramide for acid aspiration prophylaxis in elective surgery. *Anesthesiology* 1984; **61:** 48–54.
21. Bakke OM, Segura J. The absorption and elimination of metoclopramide in three animal species. *Journal of Pharmacy and Pharmacology* 1976; **28:** 32–9.
22. Assaf RAF, Dundee JW, Samuel IO. The efficacy of metoclopramide against narcotic-induced emetic symptoms. *British Journal of Clinical Pharmacology* 1974; **1:** 177P.
23. Dundee JW, Clarke RSJ. The premedicant and anti-emetic action of metoclopramide. *Postgraduate Medical Journal* 1973; **49** (July Suppl 4): 34–7.
24. Ellis FR, Spence AA. Clinical trials of metoclopramide (Maxolon) as an antiemetic in anaesthesia. *Anaesthesia* 1970; **25:** 368–71.
25. Brock-Utne JG, Dimopoulos GE, Downing JW, Moshal MG. Effect of metoclopramide given before atropine sulphate on lower oesophageal sphincter tone. *South African Medical Journal* 1982; **61:** 465–7.

Anaesthesia, 1986, Volume 41, pages 493–498

Comparison of effects of fentanyl and alfentanil on intra-ocular pressure

A double-blind controlled trial

S. M. MOSTAFA, A. LOCKHART, D. KUMAR AND M. BAYOUMI

Summary

The effects of fentanyl and alfentanil on intra-ocular pressure during anaesthesia were investigated in 50 consecutive patients in a double-blind controlled trial. Both drugs produced a significant reduction in intra-ocular pressure ($p < 0.01$). Alfentanil produced significantly greater reduction (48.5 percent) than fentanyl (28.6 percent) ($p < 0.01$). A small but statistically significant reduction in arterial pressure (15 percent approximately) and heart rate (18 percent approximately), were observed with both agents, but no significant differences between them were noted. It is suggested that alfentanil may be a suitable alternative to fentanyl in ophthalmic anaesthesia.

Key words

Analgesics; alfentanil, fentanyl.
Measurement techniques; intra-ocular pressure, tonometry.

Control of intra-ocular pressure (IOP) during ophthalmic operations, particularly intra-ocular procedures, may be an important component of satisfactory operating conditions and successful surgery.[1] Anaesthetic techniques with a tendency to lower or prevent an elevation of IOP may minimise vascular congestion of the eye and its contents.[2] Most central nervous system depressants, including narcotic analgesics, cause a reduction in IOP[3–10] and fentanyl is often used in the anaesthetic technique for intra-ocular surgery.[3,8,11–15] Alfentanil is a recently introduced, short-acting opioid analgesic.[16,17] It has a more rapid onset of action, shorter duration of effect and more rapid recovery than fentanyl.[16–19]

A pilot study in our hospital, in patients undergoing general surgery, demonstrated that alfentanil produced a reduction in IOP. The effects of any new anaesthetic on IOP should be assessed before the drug can be recommended for routine use in ophthalmic surgery. This investigation was therefore undertaken to compare the effects of alfentanil and fentanyl on IOP in a controlled, double-blind trial.

Method

The study was approved by the district medical ethics committee. Fifty consecutive adult patients (18 males and 32 females) aged 23–90 years, undergoing routine ophthalmic operations under general anaesthesia, were investigated. The anaesthetist visited all patients pre-operatively to assess their fitness and to obtain written informed

---

S.M. Mostafa, MB, ChB, FFARCS, Consultant Anaesthetist, A. Lockhart, MB, ChB, FFARCS, Senior Registrar, D. Kumar, MB, ChB, DO, FRCS, Consultant Surgeon, M. Bayoumi, MB ChB, FFARCS, Registrar, Selly Oak Hospital, Birmingham B29 6JD.

0003–2409/86/050493 + 06 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

consent. Only patients of ASA class 1 and 2 were included in the trial. Patients were randomly allocated to one of two groups, to receive fentanyl or alfentanil intra-operatively for analgesia.

IOP measurement

All IOP measurements were performed by the same investigator (DK) using a standard, hand held Perkins applanation tonometer,[20] following the application of 1–2 drops of benoxinate 0.4 percent solution and fluorescein from a dye impregnated paper strip. Intra-ocular pressure was measured in the supine position on the unoperated, normal eye (defined as an eye with pre-operative IOP of 22 mmHg or less[10]). Approximately 10 minutes after general anaesthesia and controlled ventilation were established, control IOP, heart rate and arterial blood pressure measurements were taken. At that time, end tidal carbon dioxide concentration was 5 per cent, IOP was the same (SD 1 mmHg) as pre-operative values, the heart rate and arterial blood pressure were steady and equal to pre-induction levels. The patient was then given 0.1 ml/kg of the study drug (equivalent to 2.5 and 10 μg/kg of fentanyl or alfentanil, respectively). Intra-ocular pressure, heart rate and blood pressure were then measured simultaneously at 1, 2.5, 5, 7.5, 10 and 15 minutes following the administration of the trial drug. Thereafter, no further measurement of IOP was performed and the study was terminated.

Anaesthesia

All patients were premedicated with diazepam 5–10 mg orally 2 hours pre-operatively. This is believed to cause no significant change in IOP.[21] Induction of anaesthesia was with thiopentone 3–4 mg/kg, followed by alcuronium 0.3 mg/kg. Alcuronium was chosen to prevent any significant alteration of IOP.[22] Inflation of the lungs with oxygen, laryngoscopy and spraying of the vocal cords with 1.5 mg/kg lignocaine were performed after satisfactory muscle relaxation was achieved. None of the patients showed any movement during intubation of the trachea with size 8 or 9 mm cuffed Magill tracheal tubes.

Ventilation of the lungs was controlled using a mixture of 34 percent oxygen in nitrous oxide fed into the delivery tube of a Bain type co-axial breathing circuit.[23] Fresh gas flow from the anaesthetic machine was adjusted to deliver a total gas flow as close to 70 ml/kg/minute as the flowmeter etchings permitted, as this flow rate has been shown to produce normocapnia during controlled ventilation.[24] A Nuffield 200 ventilator (Penlon Co. Ltd.) was used to control ventilation. In order to maintain the mean intrathoracic pressure as low as possible during controlled ventilation, and to maintain optimal ventilation of the lungs during anaesthesia, the tidal volume was adjusted to about 10–12 ml/kg with a respiratory frequency of 13/minute.

Surgery commenced when the study period was completed and anaesthesia continued with nitrous oxide, oxygen and halothane 0.5%. Halfway through the operation, the patients were given droperidol 5 mg intravenously as an anti-emetic. Residual neuromuscular blockade was antagonised at the end of the operation with neostigmine and atropine, 50 μg and 20 μg/kg respectively.

Expired tidal and minute volumes were checked by inserting an electronic Wright's respirometer[25] (BOC, Medishield Ltd., U.K.), between the catheter mount and the breathing system. End-tidal carbon dioxide concentration was monitored continuously by a calibrated Datex infrared carbon dioxide analyser (Vickers Medical, U.K.) with an accuracy of ± 0.1 percent and maintained throughout the trial period at 5 percent by the addition, if needed, of carbon dioxide to the fresh gas supply and adjusting the flow rates of oxygen and nitrous oxide appropriately to maintain oxygen concentration. Heart rate and rhythm were continuously monitored by an electrocardiogram (ECG). Arterial blood pressure was measured using an automatic blood pressure monitor (Sentron, Bard, Critical Care Division, UK).

Changes in IOP, systolic and diastolic pressures, and heart rate within groups were analysed by means of the two-way analysis of variance, using the Greenhouse and Geisser technique.[26] Comparisons between groups were first analysed by carrying out split-plot analysis of variance on the change from control value with all four variables.[27] This analysis showed statistically insignificant time-by-treatment interaction. Consequently, the mean change from control value for each of the four variables over the study period for each group was calculated and a one-way analysis of variance on these data was performed. Results which showed a significant group effect with respect to a mean change were analysed by the two sample *t*-test. The two sample *t*-tests were performed on the absolute changes in IOP, systolic and diastolic pressures and heart rate.

Results

Physical characteristics of patients are summarised in Table 1. There were no significant differences between the mean age, weight or sex distribution of patients in the two groups. Few patients in both groups were suffering from concommittant physical conditions such as hypertension, diabetes, asthma and angina pectoris. Their condition was stable and they were receiving a variety of drugs, including antihypertensive agents and bronchodilators. The majority of operations were cataract extractions (70 percent) and dacryocystorhinostomy (12 percent).

Table 1. Patients details (SEM)

Group	Age (years)	Weight (kg)	Sex
Fentanyl	65.2	7.8	M:9
	(2.7)	(2.9)	F:16
Alfentanil	70.4	68.3	M:9
	(1.4)	(2.6)	F:16

There were no significant differences between the mean control IOP, systolic and diastolic pressures and heart rate in the two groups (Table 2). The mean change in these four variables are also shown in Table 2. When the results for each of these four variables within each group were analysed, using the two-way analysis of variance, significant mean falls in IOP, systolic and diastolic pressures and heart rate were found in both treatment groups ($p<0.01$, $F = 13.01$ or more, df 24 and 174).

Comparison of the mean change, from control value, in IOP between groups, using one-way analysis of variance, was made. This analysis showed that mean IOP fell significantly more in the alfentanil group than the fentanyl group ($p<0.01$, $F = 17.85$, *df* 1 and 49). Accordingly, comparisons between groups were made, using the two-sample *t*-tests. Alfentanil, consistently appeared to cause a significantly greater reduction in IOP than fentanyl during the study period ($p<0.001$; Fig. 1).

Comparisons of the mean change in systolic and diastolic pressures and heart rate using one-

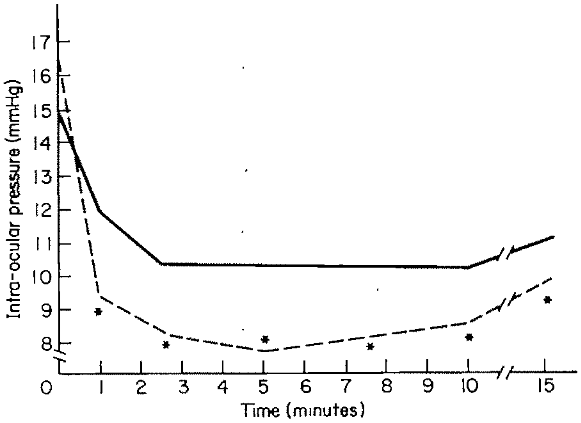


Fig. 1. Mean intra-ocular pressure in each group in relation to time. *, significantly greater decrease than after fentanyl ($p<0.01$); ——, fentanyl; ----. alfentanil.

Table 2. Mean control value and reduction in IOP (mmHg) following fentanyl and alfentanil administration (SEM).

Group	*n*	Control value	Time after treatment (minutes) 1	2.5	5	7.5	10	15	Mean overall change
Fentanyl	25	15	2.9	4.7	4.6	4.6	4.8	3.9	4.3
		(0.95)	(0.57)	(0.55)	(0.69)	(0.69)	(0.73)	(0.86)	
Alfentanil	25	16.7	7.3*	8.4*	7.3*	9*	8.2*	6.9*	8.1†
		(0.84)	(0.86)	(0.83)	(0.86)	(0.75)	(0.75)	(0.91)	

*†Significantly lower than fentanyl; $p<0.001$ and $p<0.01$ respectively.

Table 3. Mean control value and reduction in systolic, diastolic pressure (mmHg) and heart rate (beats/minute) following fentanyl and alfentanil administration (SEM)

Variable	Group	*n*	Control value	Time after treatment (minutes)						Mean overall change
				1	2.5	5	7.5	10	15	
Systolic pressure	Fentanyl	25	140.3 (2.86)	7.8 (2.8)	13.6 (4.5)	22.2 (4)	24.4 (3.7)	25 (3.7)	24.5 (3.5)	19.6*
	Alfentanil	25	147 (4.82)	9.2 (2.8)	22.7 (2.8)	26.4 (2.2)	24.2 (2.5)	24.9 (2.7)	22.2 (2.7)	21.6*
Diastolic pressure	Fentanyl	25	83.5 (2.36)	2.3 (1.6)	10.8 (2.7)	14.8 (2.6)	16.4 (2.9)	16.2 (2.7)	15.7 (2.7)	12.7*
	Alfentanil	25	83.8 (2.6)	4.4 (1.8)	14.8 (1.5)	14.7 (1.5)	13.8 (1.7)	15.7 (1.6)	13.8 (1.9)	12.9*
Heart rate	Fentanyl	25	79.7 (2.42)	5.2 (1.2)	11.6 (1.5)	15.2 (1.5)	18.3 (1.6)	18.2 (1.5)	18.3 (1.6)	14.5*
	Alfentanil	25	81.6 (2.24)	7.8 (1.4)	15.1 (1.8)	16.7 (1.3)	16.7 (1.3)	16.4 (1.4)	16.5 (1.5)	14.9*

*Significant fall from control value; $p<0.01$.

way analysis of variance were made (Table 3). There were no significant differences between the groups ($p>0.05$, $F=0.27$, 0.1, 0.05 for systolic and diastolic pressures and heart rate respectively). However, four patients developed bradycardia (heart rate <50 beats/minute). Three patients were in the fentanyl group and one in the alfentanil group.

Satisfactory operating conditions in both groups were reported by the surgeons. Postoperatively, there was no vomiting and no systemic complications in any of the patients. All patients recovered consciousness and adequate respiratory function within 10 minutes of the end of anaesthesia.

Discussion

The use of modern surgical techniques has made general anaesthesia an increasingly popular choice in ophthalmic surgery. Patients presenting for cataract extraction, surgical treatment for glaucoma and other ocular disease are frequently old and frail and may have limited cardiopulmonary reserve. These patients require anaesthetic techniques which provide stable intra-ocular and haemodynamic conditions during operation.[28,29] Providing such conditions has engaged the attention of anaesthetists for many years and the subject was reviewed recently.[8] A technique similar to ours, using fentanyl and controlled ventilation has been described as useful in providing good conditions for the surgeons and smooth recovery from anaesthesia. Fentanyl is also reported to provide good analgesia, has few adverse effects on the circulation and helps to prevent coughing when the tracheal tube is removed.[8] In addition, it is reported to produce moderate reduction of IOP.[3,8,11–15] Our results appear to confirm such reports. Over the study period, a mean reduction in IOP of 28.6 percent (range 19.3–32 percent) was noted in the fentanyl group. However, while fentanyl may exhibit many desirable characteristics, it is also reported to have a slower elimination half-life than alfentanil.[18,30] Also, the duration of narcotic effect of multiple doses of fentanyl may be prolonged and difficult to assess by the anaesthetist[30]; respiratory depression may occur during the recovery period.[31]

Alfentanil is reported to have a more rapid onset of action and less cumulation than fentanyl.[16–18,30,31] Recovery from alfentanil is faster than with fentanyl[19] or even halothane.[32] Alfentanil is also reported to cause a significantly lower incidence of postoperative vomiting than fentanyl.[33] None of our patients vomited postoperatively. This may have been due to the potent anti-emetic action of droperidol given routinely to all our patients undergoing ophthalmic surgery.

We know of no reports describing the effects of alfentanil on IOP. In common with other narcotic analgesics, our results show that, over the study period, alfentanil produced a significant reduction in baseline IOP (48.5 percent, range 41.3–53.9 percent). Furthermore, although the doses of fentanyl and alfentanil used in this study are reported to be equipotent,[16,34,35] the latter produced a significantly greater reduction in IOP than the former ($p<0.01$). The magnitude of reduction in IOP was similar to, and on occasions higher than, that reported for halothane.[28] In addition, the maximum reduction in IOP occurred at 5 and 10 minutes in the alfentanil and fentanyl groups respectively (Fig. 1). This may highlight the speed of action of alfentanil compared with fentanyl.

All our IOP measurements were made in the supine position, which may have caused some rise in IOP. A further rise in IOP may have occurred with controlled ventilation of the lungs. However, inflation pressures were low (2.0–2.5 kPa) and constant for each patient. Furthermore, the anaesthetic technique was standardised and factors known to influence IOP were controlled.[6]

The possible mechanisms by which alfentanil reduces IOP are probably similar to those of other central nervous system depressants.[1] These include relaxation of intra- or extra-ocular muscles, facilitation of flow of aqueous humour or a decrease in its production. It may also be due to the decrease in blood pressure observed in this study. However, the decrease in arterial pressure, although statistically significant in both groups, was small (15 percent approximately in each group) and did not require any clinical intervention by the anaesthetist to restore it to pretreatment value. Furthermore, there were no statistically significant differences between the alfentanil and fentanyl groups with respect to arterial pressures. It may therefore be reasonable to suggest that the decrease in arterial pressure contributed only a small part in reducing IOP in the alfentanil group.

With respect to heart rate changes in the two groups, again, although there was significant reduction in the two groups, these were small (18 percent approximately in each group) and did not necessitate treatment; no signficant differences were noted between the groups. Of the patients who developed bradycardia, two in the fentanyl group were receiving reserpine and atenolol and one patient in the alfentanil group was taking quinine sulphate. None of these patients required treatment, since they were clinically stable and the bradycardia was transient.

The use of inhalation agents, particularly in the elderly, may be accompanied by cardiovascular depression, substantial hypotension[8,13,29,36,37] and may sensitise the heart to the action of exogenous catecholamines, such as phenylephrine, used in ophthalmic anaesthesia.[38] The elimination of coughing (necessary to prevent a rise in IOP postoperatively) may also be difficult to achieve with some inhalation agents.[10]

Alfentanil may be particularly useful in patients in whom the action of fentanyl is considered to be prolonged, or in whom rapid suppression of the reflex responses to surgery is required.[39] Its effects on IOP reported here suggest that its use in patients undergoing ophthalmic surgery may be advantageous. Patients in whom it is desirable to avoid the risk of cardiovascular depression (such as those with pre-existing cardiovascular disease), repeat halothane anaesthesia and those undergoing short procedures (e.g. iridectomy), may benefit from the use of alfentanil during anaesthesia.

In conclusion, alfentanil appears significantly to reduce IOP during anaesthesia with nitrous oxide/oxygen, controlled ventilation and normocapnia. This reduction is significantly greater than that following fentanyl. Alfentanil appears to be a reasonable alternative to fentanyl and a useful agent in the armamentarium of anaesthetists during anaesthesia for ophthalmic surgery.

Acknowledgments

We would like to thank Mrs L. Ingram for her secretarial help, Miss H. Waldren and Miss A. Whitehead, Janssen Pharmaceuticals Ltd, for supplying the drugs and statistical analysis for the trial. We would also like to thank Mr J. Appleby and the District Information Services, South Birmingham Health District, for assistance in the preparation of the statistics.

References

1. Duncalf D, Foldes FF. Effect of anesthetic drugs and muscle relaxants on intraocular pressure. *Internctional Ophthalmology Clinics* 1973; **13:** 21–33.
2. Duncalf D, Rhodes DH Jr. *Anesthesia in clinical ophthalmology.* Baltimore: Williams and Wilkins, 1963: 11.
3. Pöntinen PJ, Miettinen P, Reinikainen M. Neuroleptanalgesia in cataract surgery II. *Acta Ophthalmologica (Kobenharn)* 1966; Suppl. 80: 1–36.
4. Beaugie A, Samuel JR. Some observations on the effect of carbon dioxide on intraocular pressure in man. *British Journal of Anaesthesia* 1973; **45:** 119.
5. Al-Abrak MH, Samuel JR. Effects of general anaesthesia on the intraocular pressure in man. Comparison of tubocurarine and pancuronium

in nitrous oxide and oxygen. *British Journal of Ophthalmology* 1974; **58:** 806–10.

6. Al-Abrak MH, Samuel JR. Further observations on the effects of general anaesthesia on intraocular pressure in man: halothane in nitrous oxide and oxygen. *British Journal of Anaesthesia* 1974; **46:** 756–9.
7. Al-Abrak MH, Samuel JR. Effects of general anaesthesia on the intraocular pressure in man: trichlorethylene in nitrous oxide and oxygen. *British Journal of Ophthalmology* 1975; **59:** 107–10.
8. Adams AK, Jones RM. Anaesthesia for eye surgery: general considerations. *British Journal of Anaesthesia* 1980; **52:** 663–8.
9. Holloway KB. Control of the eye during general anaesthesia for intraocular surgery. *British Journal of Anaesthesia* 1980; **52:** 671–8.
10. Utting JE. Anaesthesia for ophthalmic surgery In: *General anaesthesia,* 4th Edn, Volume 2. Gray TC, Nunn JF, Utting JE, eds. London: Butterworths 1980: 1205.
11. Marynen L, Libert K. Ocular tonometry in the child under general anesthesia with IM ketamine. *Acta Anaesthesiologica Belgica* 1976; **27** (Suppl.): 29–40.
12. Pearce JL. General and local anaesthesia in eye surgery. *Transactions of the Ophthalmological Societies of the United Kingdom* 1982; **102:** 31–4.
13. Smith GB. *Ophthalmic anaesthesia.* London: Edward Arnold, 1983: 32.
14. Smith RB, Leaño N. Intraocular pressure following pancuronium. *Canadian Anaesthetists' Society Journal* 1973; **20:** 742–6.
15. Sia RL, Rashkovsky OM. OrgNC45 and intraocular pressure during anesthesia. *Acta Anaesthesiologica Scandinavica* 1981; **25:** 219–21.
16. De Castro J, Van de Water A, Wouters L, Xhonneux R, Reneman R, Kay B. Comparative study of cardiovascular, neurological and metabolic side effects of eight narcotics in dogs. *Acta Anaesthesiologica Belgica* 1979; **30:** 5–54.
17. Cookson RF, Niemegeers CJE, Vanden Bussche G. The development of alfentanil. *British Journal of Anaesthesia* 1983; **55:** 147S–55S.
18. Bower S, Hull CJ. Comparative pharmacokinetics of fentanyl and alfentanil. *British Journal of Anaesthesia* 1982; **54:** 871–7.
19. Kay B, Venkataraman P. Recovery after fentanyl and alfentanil in anaesthesia for minor surgery. *British Journal of Anaesthesia* 1983; **55:** 169S–71S.
20. Perkins ES. Hand-held aplanation tonometer. *British Journal of Ophthalmology* 1965; **49:** 591–3.
21. Trew CT, Manus NJ, Jackson DM. Intra-ocular pressure and premedication with oral diazepam. *Anaesthesia* 1982; **37:** 339–40.
22. George R, Nursingh A, Downing JW, Welsh NH. Non-depolarizing neuromuscular blockers and the eye: A study of intraocular pressure. *British Journal of Anaesthesia* 1979; **51:** 789–92.
23. Bain J, Sporrel WE. Flow requirements for modified Mapleson D system during controlled ventilation. *Canadian Anaesthetists' Society Journal* 1973; **20:** 629–36.
24. Henville JD, Adams AP. The Bain anaesthetic system. An assessment during controlled ventilation. *Anaesthesia* 1976; **31:** 247–56.
25. Conway CM, Leigh JM, Preston TD, Walters FJM, Webb DA. An assessment of three electronic respirometers. *British Journal of Anaesthesia* 1974; **46:** 885–91.
26. Greenhouse SW, Geisser R. On methods in the analysis of profile data. *Psychometrica* 1954; **24:** 95–112.
27. Gill JL, Hafs HD. Analysis of repeated measurements of animals. *Journal of Animal Science* 1971; **33:** 331–6.
28. Adams AP, Freedman A, Henville JD. Normocapnic anaesthesia for intraocular surgery. *British Journal of Ophthalmology* 1979; **63:** 204–10.
29. Norbury A, Rocke AD, Brock-Utne JG, Mackenzie R, Welsh N, Downing JW. Balanced total intravenous anaesthesia and intraocular pressure. *Anaesthesia and Intensive Care* 1981; **9:** 255–9.
30. Stanski DR, Hug CC Jr. Alfentanil—a kinetically predictable narcotic analgesia (Editorial). *Anaesthesiology* 1982; **57:** 435–8.
31. Hull CJ. The pharmacokinetics of alfentanil in man. *British Journal of Anaesthesia* 1983; **55:** 157S–64S.
32. Antonios WRA, Inglis MD, Lees NW. Alfentanil in minor gynaecological surgery: use with etomidate and a comparison with halothane. *Anaesthesia* 1984; **39:** 812–5.
33. Patrick M, Eagar B, Toft DF, Sebel PS. Alfentanil supplemented anesthesia for short procedures: a double blind comparison with fentanyl. *Anesthesiology* 1983; **59:** A346.
34. Kay B, Cohen AT, Shaw F, Healy TEJ. Anaesthesia for laparoscopy: alfentanil and fentanyl compared. *Annals of the Royal College of Surgeons of England* 1983; **65:** 316–7.
35. Black TE, Kay B, Healy TEJ. Reducing the haemodynamic responses to laryngoscopy and intubation. A comparison of alfentanil with fentanyl. *Anaesthesia* 1984; **39:** 883–7.
36. Rose NM, Adams AP. Normocapnic anaesthesia with enflurane for intraocular surgery. *Anaesthesia* 1980; **35:** 569–75.
37. Runciman JC, Bowen-Wright RM, Welsh NH, Downing JW. Intra-ocular pressure changes during halothane and enflurane anaesthesia. *British Journal of Anaesthesia* 1978; **50:** 371–4.
38. Burn RA, Knight P. Anaesthesia in ophthalmic surgery. *British Journal of Hospital Medicine* 1969; **2:** 1527–44.
39. Kay B. (Editorial). Alfentanil. *British Journal of Anaesthesia* 1982; **54:** 1011–3.

Anaesthesia, 1986, Volume 41, pages 499–504

Caudal analgesia for perianal surgery

A comparison between bupivacaine and diamorphine

P. M. BAILEY AND S. SANGWAN

Summary

Seventy-three patients undergoing elective perianal surgery were randomly divided into a control group, a group who received a caudal injection of 20 ml bupivacaine 0.5% plain and a group who received diamorphine 2.5 mg in 10 ml normal saline by caudal injection; a comparison was then made of postoperative analgesia requirements. The bupivacaine group had better analgesia than the control group for the first 8 hours, after which there was no difference. The diamorphine group had better analgesia than the control group for the first 24 hours postoperatively. Side effects were less in the diamorphine group than the control, or the bupivacaine group. In particular, 41% of the bupivacaine group complained of some degree of urinary retention and one patient required temporary catheterisation. It is concluded that caudal diamorphine gives good postoperative analgesia for perianal operations, particularly when motor blockade is not wanted by the surgeon.

Key words

Analgesia; postoperative.
Anaesthetic techniques; epidural, caudal, narcotics.

Epidural or intrathecal opiates are now widely used for postoperative analgesia,[1,2] following the first description of their use by these routes.[3-5] Reports about opiate receptor sites[6-8] have indicated the substantia gelatinosa as the main site of action. Others have shown the existence of opiate receptor sites on the dorsal roots of nerves[9] and reports from other studies have suggested the effectiveness of opiates given more peripherally.[10,11] Farag and Naguib[12] have recently reported on the postoperative analgesia given by caudal morphine injected at the end of surgery.

This trial was designed to compare the effectiveness in providing postoperative analgesia, of diamorphine given by the caudal route to a local anaesthetic (bupivacaine) given by the caudal route, and in comparison to a control group who received no caudal analgesia.

Some surgeons prefer not to use caudal injections of a local anaesthetic agent for perianal surgery because muscle tone may be lost.

P.M. Bailey,* MB, BS, FFARCS, S. Sangwan,† MB, BS, FFARCS, Department of Anaesthesia, St Mark's Hospital for Diseases of the Colon and Rectum, City Road, London, EC1.
Present addresses:
*Department of Anaesthesia, University College Hospital, Gower Street, London, WC1.
†Department of Anaesthesia, The London Hospital, Whitechapel, London, E1.

0003–2409/86/050499 + 06 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Epidural diamorphine by the caudal route may offer an alternative method of analgesia for long duration, without motor blockade or the need for repeated intramuscular opiates which may cause problems of constipation.

Methods

Seventy-three patients presenting for elective surgery for haemorrhoids, fissure-in-ano, or fistula were randomly allocated to three groups A, B and C. All patients were in ASA groups 1 and 2, between the ages of 18 and 65 years and gave their informed consent pre-operatively, when the method of postoperative pain scoring was explained to them. Approval for the study was obtained from the district ethical committee.

All patients received premedication of papaveretum (Omnopon) 0.3 mg/kg and hyoscine (Scopolamine) 0.005 mg/kg by intramuscular injection, 1.5 hours pre-operatively.

Anaesthesia was induced with thiopentone 4–6 mg/kg. Patients in group A had anaesthesia maintained with oxygen, nitrous oxide and halothane, breathed spontaneously and formed the control group. Patients in group B were given a caudal injection of 20 ml bupivacaine hydrochloride 0.5% plain, after induction and thereafter anaesthesia was by spontaneous ventilation with oxygen, nitrous oxide and halothane. Patients in group C received a caudal injection of diamorphine hydrochloride 2.5 mg in 10 ml normal saline after induction of anaesthesia and anaesthesia was maintained by spontaneous ventilation with oxygen, nitrous oxide and halothane.

Pulse rate and electrocardiogram (ECG) were continuously monitored by cardioscope. Systolic and diastolic blood pressures were monitored by an automatic recorder. (Dinamap, Critikon) and respiratory rate and expired carbon dioxide concentration were monitored by Datascope capnograph sampling from the anaesthetic mask. These measurements were noted after induction, at the commencement of surgery and, thereafter, at 5-minute intervals throughout the operation.

The concentration of halothane required to maintain adequate anaesthesia was noted in all patients. Recovery was followed by noting the time taken from the end of the anaesthetic until the patients opened their eyes to command and then gave their correct date of birth. All patients were prescribed papaveretum 0.3 mg/kg by intramuscular injection for postoperative pain relief, which they could receive 4-hourly as required.

Before returning to the ward after full recovery, all patients were asked by the recovery room staff to score their pain on a standard 10-cm linear analogue scale and this was repeated by the ward nurses at 2 hours postoperatively and then every 4 hours, except when the patient was sleeping, for the first 24 hours postoperatively. On the first postoperative day, the patient was visited by an independent assessor and both the patient and the ward staff were asked to assess pain relief as poor, good or excellent. Any side effects were noted, particularly hypotension, respiratory depression, pruritus, urinary retention, nausea, paraesthesia and motor blockade. The time from full recovery until the first dose of postoperative analgesia was noted, as was the total analgesia requirement for the first 24 hours.

The mean pain scores were compared by Student's *t*-test and $p < 0.05$ was taken as significant.

Results

Twenty-eight patients were allocated to group A (the control group), twenty-six patients were allocated to group B (caudal injection of bupivacaine) and twenty-six patients were allocated to group C (caudal injection of diamorphine). The three groups were broadly matched for age, sex, weight and type of operation (Tables 1 and 2).

Out of 42 caudal blocks attempted, seven were

Table 1. General characteristics of patients

	Group A (control)			Group B (bupivacaine 20 ml 0.5%)			Group C (diamorphine 2.5 mg)		
	Number of patients	Age and weight (means)		Number of patients	Age and weight (means)		Number of patients	Age and weight (means)	
		(years)	(kg)		(years)	(kg)		(years)	(kg)
Male	17	46.6	70.4	16	45.2	70.3	13	42.3	74.3
Female	11	50.2	64.1	8	37	58.6	8	39	59.8

Table 2. Nature of operations.

	Group A control (%) ($n = 28$)	Group B bupivacaine (%) ($n = 24$)	Group C diamorphine (%) ($n = 21$)
Haemorrhoidectomy	68	55	58
Lay-open-fistula	21	33	26
Lateral anal sphincterotomy	11	12	16

technically impossible (16% failure) and these patients were excluded from the trial, thus reducing the numbers in groups B and C after random allocation. This failure rate is similar to other studies.[11,13] The mean pain scores for the three groups were assessed by a linear analogue scale[14] at intervals over the first 24 hours postoperatively (Fig. 1). Group B, the bupivacaine group, had significantly lower pain scores than the control group A for the first 8 hours postoperatively ($p < 0.01$). After this time, there was no significant difference between group B and group A. Group C, the diamorphine group, had significantly lower pain scores than the control group A for the first 8 postoperative hours ($p < 0.01$). At 12 and 16 hours postoperatively, the mean pain scores were lower than group A, but did not achieve statistical significance. At 20 and 24 hours, the mean pain scores of group C were again significantly less than group A ($p < 0.05$ and $p < 0.01$ respectively),

Between groups B and C there was no significant difference in mean pain scores in the recovery room. Group B had significantly lower pain scores at 2 and 4 hours postoperatively ($p < 0.05$) but there was no difference at 8 hours. At 12 hours, group C was significantly lower than group B ($p < 0.05$). While there was no difference at 16 and 20 hours, group C was significantly lower than group B at 24 hours ($p < 0.01$).

Table 3 shows the requirements for postoperative analgesia in the first 24 hours for the three groups. In group A, six patients (21.5%) required no postoperative analgesia compared with eight patients in group B (33%); this was significantly different ($p < 0.05$) (Table 3). In group C, fourteen patients (64.7%) required no analgesic injections in the first 24 hours, which was significantly more than groups A and B ($p < 0.01$). Of the patients who required some analgesia postoperatively, group B patients required significantly fewer injections than group A patients ($p < 0.05$) and group C patients required significantly fewer injections than group B patients ($p < 0.05$). No patients in either group

Table 3. Intramuscular analgesic requirements in the first 24 hours postoperatively.

	Group A ($n = 28$)	Group B ($n = 24$)	Group C ($n = 21$)
No analgesics at all	6 (21.5%)	8 (33%)*	14 (64.7%)†
One injection	11 (39.2%)	7 (29.5%)	2 (8.8%)
Two injections	6 (21.5%)	9 (37.5%)	5 (20.5%)
Three injections	5 (17.8%)	0	0
More than three injections	0	0	0

*$p < 0.05$ for group A, compared to group B.
**$p < 0.01$ for group C compared to groups A and B.

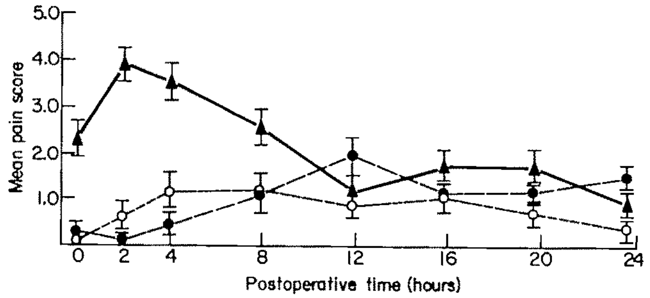


Fig. 1. Pain scores during the first 24 hours (mean, SEM), ▲—▲, Control group A; ●—●, bupivacaine group B; ○---○, diamorphine group C.

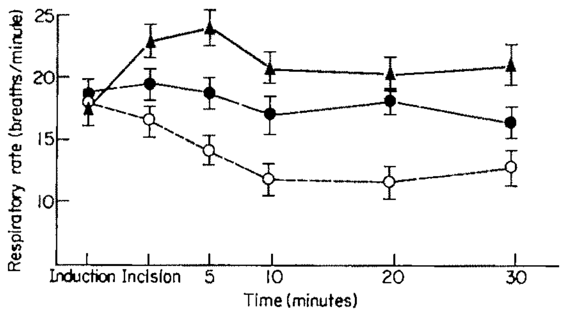


Fig. 2. Respiratory rate during surgery (mean SEM), ▲—▲, Control group A; ●—●, bupivacaine group B; ○---○, diamorphine group C.

B or C required more than two injections, while five patients in group A (17.8%) required three injections.

During the operative procedure, there was no significant difference between, or overall change in, the pulse rate and blood pressures of group B and C patients. The pulse rate and blood pressure of group A patients showed an initial rise during the first 5 minutes, but this was not statistically different.

Figures 2 and 3 show the respiratory rate and percentage expired carbon dioxide concentration during the operative procedure. Patients in group B had no significant change in respiratory rate during the procedure. Patients in group A had a large increase in respiratory rate at the beginning of surgery which, although reduced after 5 minutes, remained significantly greater than patients in group B ($p<0.01$). Group C patients showed a fall in respiratory rate for the first 10 minutes, and remained significantly lower than group B throughout the procedure ($p<0.01$).

In group A patients (Fig. 3), there was an initial fall in expired carbon dioxide concentration in relation to group C, ($p<0.05$) although there was no statistically significant fall within the group and the carbon dioxide concentration remained at a constant level throughout the procedure. The carbon dioxide concentration in group B patients did not decrease with the incision, but gradually rose throughout the surgical procedure; the level was significantly greater than group A at incision, at 5 minutes, 20 minutes and 30 minutes ($p<0.01$). Group C patients showed a rise in carbon dioxide concentration for the first 10 minutes, after which it remained steady at a significantly greater level than group A throughout the procedure ($p<0.01$), but was not significantly different from group B until after 10 minutes ($p<0.01$, and reverted to normal on wakening.

The time from cessation of the anaesthetic until opening the eyes to command was less in group B (15.4 minutes, SEM 1.1 minutes) than group A (17.3 minutes, SEM 1.1 minutes) and C (17.9 minutes, SEM 1.1 minutes) though not statistically significant, while the total

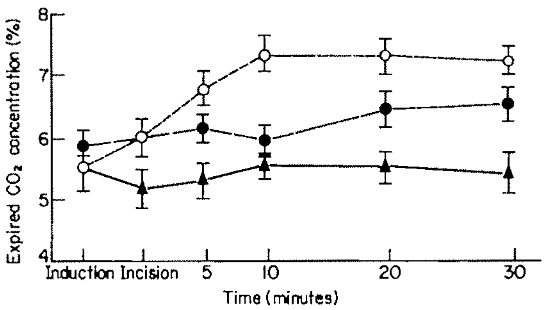


Fig. 3. Expired carbon dioxide concentration (mean; SEM) during surgery. ▲—▲, Control group A; ●—●, bupivacaine group B; ○---○, diamorphine group C.

recovery time, taken as the mean times to give their correct date of birth, was significantly shorter for group B (23 minutes, SEM 1.4 minutes) than groups A (30 minutes, SEM 1.9 minutes) and C (29.5 minutes, SEM 1.9 minutes) ($p < 0.01$).

During the procedure, five patients in group A (18%) developed abnormalities on ECG, three patients had atrial extrasystoles (one had coupled beats throughout the procedure) and two had ventricular ectopic beats. In group C, two patients (9%) showed ECG irregularities; one patient had a junctional rhythm throughout and one had atrial ectopics. No patients in group B showed any ECG irregularities. Eleven patients in group A (39%) complained of nausea and required intramuscular anti-emetics, compared with seven patients in group B (29%) and seven patients in group C (32%).

No patient in the trial developed postoperative respiratory depression. The intra-operative respiratory depression seen in group C patients returned to normal as they awoke. No patients complained of pruritus. Eight patients (33%) in group B noticed some paraesthesia and seven patients (29%) also in group B, noted a degree of motor blockade. The majority of these patients accepted this, but three patients (two female, one male) found it distressing. No patients in groups A or C suffered from this. Ten patients in group B (41%) complained of some urinary retention postoperatively. This manifested itself mainly as hesitancy on micturition, but one man required temporary catheterisation. No patients in groups A or C complained of this.

Discussion

The caudal injection of a local anaesthetic agent is a simple and widely used method of giving good pre-operative and postoperative analgesia. Opiates have been given both intrathecally and extradurally and shown to give good postoperative analgesia for long periods.[2,15,16] Research into receptor locations has shown that opiates enter the substantia gelatinosa of the spinal cord to produce their effect.[6-8] It has been thought that both epidural and intrathecal opiates have this common site of action, with epidural opiates having to cross the spinal dural membrane and enter the cerebrospinal fluid before binding to receptors. This accounts for their higher equipotent dose requirements over intrathecal opiates. It has been thought that any binding to peripherally sited opiate receptors was secondary to their main site of action; however, a study by Jensen[11] described the good effect of giving a caudal epidural injection of morphine for postoperative pain control, compared with intramuscular injections of opiates, for surgery below the level of the umbilicus.

The results of this study confirm the effectiveness of caudal bupivacaine for peroperative and postoperative analgesia. However, its effect was shown to last up to 8 hours postoperatively, after which there was no significant difference compared to the control group. The patients in the control group obviously feel more stimulation during surgery, as evidenced by the higher respiratory rate, lower end-tidal carbon dioxide concentration and higher halothane concentration necessary for adequate anaesthesia.

Caudal diamorphine provides effective postoperative analgesia, which was better than the control group throughout the 24 hours studied, and better than the bupivacaine group after 8 hours. Initially, there is rapid systemic absorption from the epidural space, as shown by the ventilatory depression which developed over the first 10 minutes after injection. Previous studies have also shown ventilatory depression after extradural opiates and systemic absorption has been suggested to be equivalent to intramuscular injection.[17-20] However, as the plasma half-life of intramuscular diamorphine is only 1.5–2.5 hours, the central effects of systemic absorption are unlikely to account for the long duration of analgesia shown by this study.

The alternative sites of action may be either at the substantia gelatinosa or, more peripherally, on the nerve roots as they emerge from the dura. The spinal cord ends at the L_2 level, but the dura ends at the S_2 level so that uptake of diamorphine which is very lipophilic, could occur into the cerebrospinal fluid across the dura, and then to the substantia gelatinosa of the cord. Fields *et al.*[9] have shown that the dorsal nerve roots are rich in opiate receptors and a recent report of the effectiveness of a brachial plexus block performed using morphine[21] may support the case for a more peripheral site of action of opiates, as well as at the substantia gelatinosa.

No patients showed any postoperative respiratory depression, as in previous series,[11,12] in which the caudal injections were made postoperatively, either on awake patients when they first experienced pain, or on patients who were waking, and in whom it is likely that their respiratory drive was greater than anaesthetised patients.

The incidence of cardiac dysrhythmias (group A, 18%; group B, 0%; group C, 9%) may partly be a reflection of the halothane concentration necessary for adequate anaesthesia in each group and the circulating level of catecholamines. Group A patients would be expected to have a higher circulating level of catecholamines from their response to surgical stimulation. The incidence of dysrhythmias did not correlate with the mean level of expired CO_2 concentration which was highest in group C and lowest in group A (Fig. 3).

Postoperatively, nausea was seen as a side effect in all groups in the same incidence as previously reported.[22] The bupivacaine group showed the highest incidence of side effects which were of concern to the patients; in particular, 41% complained of some degree of urinary retention.

In conclusion, this study shows that diamorphine can be given simply by the caudal route and provides more effective, long-lasting postoperative analgesia when compared to both a control group and to a group receiving bupivacaine by caudal injection. It is likely that reduced requirements for analgesics postoperatively would result not only in greater comfort for the patient, but also less opiate-induced constipation, which is beneficial in anal surgery. Caudal diamorphine is particularly suited for operations performed by surgeons who do not like the motor blockade produced by caudal bupivacaine.

Acknowledgments

The authors wish to thank Mr P.R. Hawley and Mr J.M.A. Northover for permission to study their patients and also the theatre and ward staff at St Mark's Hospital who were always helpful in performing the postoperative observations.

References

1. Cousins MJ, Mather LE, Glynn CJ, Wilson PR, Graham JR. Selective spinal analgesia. *Lancet* 1979; **1:** 1141–2.
2. Bromage PR, Camporesi E, Chestnut D. Epidural narcotics for postoperative analgesia. *Anesthesia and Analgesia* 1980; **59:** 473–80.
3. Behar M, Olswang D, Magora F, Davidson JT. Epidural morphine in treatment of pain. *Lancet* 1979; **1:** 527.
4. Yaksh TL, Rudy TA. Analgesia mediated by a direct spinal action of narcotics. *Science* 1976; **192:** 1357–8.
5. Wang JK. Analgesic effect of intrathecally administered morphine. *Regional Anaesthesia* 1977; **2:** 8–11.
6. Duggan AW, Hall JG, Headley PM. Morphine, enkephalin and the substantia gelatinosa. *Nature* 1976; **264:** 456–8.
7. Snyder SH. Opiate receptors and internal opiates. *Scientific American* 1977; **236:** 44–56.
8. Kitahata LM, Collins JG. Spinal action of narcotic analgesics. *Anesthesiology* 1981; **54:** 153–63.
9. Fields HL, Emson PC, Leigh BK, Gilbert RFT, Iverson LL. Multiple opiate receptor sites on primary afferent fibres. *Nature* 1980; **284:** 351.
10. Boskovski N, Lewinski A, Xuereb J, Mercieca V. Caudal epidural morphine for postoperative pain relief. *Anaesthesia* 1981; **36:** 67–8.
11. Jensen PJ, Siem-Jorgensen P, Bang Nielsen T, Wichmand-Nielsen H, Wintherreich E. Epidural morphine by the caudal route for postoperative pain relief. *Acta Anaesthesiologica Scandinavica* 1982; **26:** 511–3.
12. Farag H, Naguib M. Caudal morphine for pain relief following anal surgery. *Annals of the Royal College of Surgeons of England* 1985; **67:** 257–8.
13. Dawkins CJM. An analysis of the complications of extradural and caudal block. *Anaesthesia* 1969; **24:** 554–63.
14. Revill SI, Robinson JO, Rosen M, Hogg MIJ. The reliability of a linear analogue for evaluating pain. *Anaesthesia* 1976; **31:** 1191.
15. Wang JK, Nauss LA, Thomas JE. Pain relief by intrathecally applied morphine in man. *Anesthesiology* 1979; **50:** 149–5.
16. Rutter DV, Skewes DG, Morgan M. Extradural opioids for postoperative analgesia. A double-blind comparison of pethidine, fentanyl and morphine. *British Journal of Anaesthesia* 1981; **53:** 915–9.
17. Torda TA, Pybus DA, Liberman H, Clark M, Crawford M. Experimental comparison of extradural and I.M. morphine. *British Journal of Anaesthesia* 1980; **52:** 939–42.
18. Doblar DD, Muldoon SM, Abbrecht PH, Baskoff J, Watson RL. Epidural morphine following epidural local anesthesia; effect on ventilatory and airway occlusion pressure responses to CO_2. *Anesthesiology* 1981; **55:** 423–8.
19. Cooper GM, Goodman NW, Prys-Roberts C, Jacobson L, Douglas G. Ventilatory effects of extradural diamorphine. *British Journal of Anaesthesia* 1982; **54:** 239.
20. Reiz S, Westberg M. Side-effects of epidural morphine. *Lancet* 1980; **2:** 203–4.
21. Sanchez R, Nielsen H, Heslet L, Iversen AD. Case report: Neuronal blockade with morphine. A hypothesis. *Anaesthesia* 1984; **39:** 788–9.
22. Cousins MJ, Mather LE. Intrathecal and epidural administration of opioids. *Anesthesiology* 1984; **61:** 276–310.

Anaesthesia, 1986, Volume 41, pages 505–510

Influence of ketanserin pretreatment on the haemodynamic responses to sternotomy

J. N. CASHMAN, M. A. THOMPSON AND A. BENNETT

Summary

The effect of intravenous ketanserin on the pressor response to sternotomy was studied in 36 patients undergoing coronary artery surgery. Two doses of the drug (10 mg and 20 mg) were compared with a placebo injection of saline. After induction of anaesthesia, haemodynamic variables were measured until the institution of cardiopulmonary bypass. Plasma and platelet 5-hydroxyindoles and 5-hydroxytryptamine were measured in a subset of 13 patients. Ketanserin induced a dose-dependent amelioration of the pressor response to sternotomy. Plasma 5-hydroxyindoles and platelet 5-hydroxytryptamine levels did not correlate with clinical response. The increased effectiveness of the higher dose of ketanserin may be due to an effect other than serotonin antagonism.

Key words

Hormones; serotonin.
Pharmacology; serotonin antagonists.

The deleterious effects of intra-operative and postoperative arterial hypertension in patients undergoing open heart surgery remains a cause for concern, especially in patients with ischaemic heart disease undergoing coronary artery surgery. The incidence of hypertension following coronary artery surgery has been variously quoted as being between 30 and 60 percent,[1-3] whilst intra-operative hypertensive episodes may be even more common.[4] Intra-operative hypertension frequently occurs in response to specific stimuli such as nasopharyngeal or tracheal stimulation,[5] median sternotomy[5-7] and arousal.[8,9] Anaesthetic techniques based upon opioids, even in high doses, do not always inhibit the pressor response to stimuli such as median sternotomy,[6] particularly in patients with preserved left ventricular function.[10] An involvement of a variety of humoral factors including elevation of plasma levels of adrenaline or noradrenaline,[7,11] antidiuretic hormone,[12] renin and angiotensin[13-15] have all been variously suggested. The most likely of these would seem to be catecholamine release; however, it is also possible that 5-hydroxytryptamine (5-HT, serotonin) may be involved in the development of hypertension at such times. Indeed, James *et al.*[16] have proposed the existence of a cardiogenic hypertensive chemoreflex in which platelet aggregates upon coronary

---

J.N. Cashman, BSc, FFARCS, Senior Registrar, M.A. Thompson, FFARCS, Consultant, A. Bennett, BSc, Laboratory Technician, Department of Anaesthetics, United Medical and Dental Schools of Guy's and St Thomas' Hospitals, London Bridge, London SE1 9RT.

0003–2409/86/050505 + 06 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

atherosclerotic plaques in the proximal left coronary arterial system could release serotonin and trigger such a response. The use of specific humoral antagonist therapy would thus appear to be a rational and attractive approach to the maintenance of cardiovascular stability in such circumstances. Ketanserin, a quinazoline derivative, is a new serotonin receptor antagonist with a predominantly peripheral site of action; it has already been reported as effective in treating postcoronary artery surgery hypertension.[17] The present study was designed to evaluate the effectiveness of ketanserin in attenuating the hypertensive response to sternotomy.

Patients and methods

The protocol was approved by the hospital ethical committee and a total of 47 consenting male patients scheduled for elective myocardial revascularisation surgery were studied. An initial dose-finding study was performed on 11 patients and 36 patients took part in the principal double-blind study. The same anaesthetist cared for all patients. The patients were ASA 3, aged 37–74 years and weighed between 61 and 98 kg. Preoperative medication (which included beta-adrenoceptor antagonists, long acting nitrates and calcium antagonists in the majority of patients), was continued until the day of surgery. Any patient taking methysergide, tricyclic antidepressants, monoamine oxidase inhibitors, or any other drug likely to interfere with platelet serotonin uptake or release, was excluded from the study.

Pilot study

Eleven patients received a single dose of ketanserin (10, 20 or 30 mg) intravenously at the time of the sternal skin incision. Haemodynamic variables were continuously displayed during surgery and hard copy tracings obtained. As the 20-mg dose appeared to give an optimum response it was decided to compare ketanserin 10 mg and 20 mg with placebo in the principal study in a double-blind manner.

Principal study

Thirty-six patients were randomly allocated to three groups of 12 patients to receive either ketanserin 10 mg or 20 mg or a placebo injection. All patients were premedicated with oral lorazepam on the evening prior to surgery, and received intramuscular papaveretum and hyoscine 60 minutes before the anticipated time of anaesthetic induction. Anaesthesia was induced with phenoperidine 4–6 mg and etomidate 0.3 mg/kg and maintained with nitrous oxide in oxygen, supplemented by further doses of opiate and the addition of a low inspired concentration of halothane (<0.5 percent), as judged necessary by the clinical signs. Tracheal intubation and control of ventilation were facilitated by pancuronium 0.15 mg/kg. The trial drug was administered intravenously at the time of the sternal skin incision (approximately 5 minutes prior to sternotomy).

The electrocardiogram (ECG), heart rate (HR), arterial and central venous pressure were continuously displayed on an oscilloscope and hard copy tracings obtained. Relevant haemodynamic variables were recorded preoperatively at the commencement of surgery, on skin incision over the sternum, at sternotomy and 90 seconds later. In addition, the highest arterial blood pressure recorded before the commencement of cardiopulmonary bypass was noted. The need for additional agents to adjust circulatory haemodynamics (viz. hypotensive or inotropic drugs) was noted.

In a subset of 13 patients (four controls, five low dose and four high dose ketanserin patients), venous blood samples were taken for assay of serum 5-hydroxyindoles (5-HI) and platelet 5-HT levels. Blood samples were taken under stable anaesthesia, immediately after sternotomy (when the sternum had been fully distracted) and 10 minutes later (prior to full heparinsation).

Each blood sample (5 ml) was collected in a syringe containing 1 ml of acid–citrate–dextrose at room temperature and centrifuged within 2 hours at 136 g for 20 minutes. A 0.5 ml aliquot of the resultant platelet-rich plasma (PRP) was added to 0.5 ml of EDTA 0.4 percent and centrifuged at 1800 g for a further 15 minutes The supernatant was removed for plasma 5-HI assay. The residual 'button' of platelets was made up to 1 ml with distilled water, 'vortexed' to lyse the platelets and, together with the supernatant, immediately frozen in liquid nitrogen and stored at −25°C. Aliquots of PRP were analysed for platelet count on a coulter counter. Platelet and plasma samples were analysed simultaneously using the spectrofluorimetric assay of Drum-

Table 1. Patient characteristics, mean (SD)

	Control	Ketanserin (10 mg)	Ketanserin (20 mg)
Age (years)	55.3 (10.4)	58.1 (6.1)	57.0 (9.4)
Weight (kg)	79.1 (8.0)	78.0 (8.0)	75.6 (8.4)
Body surface area (sq)	1.94 (1.94)	1.92 (0.13)	1.89 (0.15)
Medication:			
Beta blocker	8/12	10/12	10/12
Nitrate	9/12	9/12	10/12
Ca antagonist	10/12	10/12	11/12

No significant difference between any parameter.

mond and Gordon.[18] Plasma serotonin concentrations are expressed as ng 5-HI/ml and platelet serotonin concentration as ng $5\text{-HT}/10^9$ platelets.

All results reported are expressed as mean (standard deviation). Statistical analysis was performed with analysis of variance and Student's *t*-test, paired or unpaired as appropriate. Values of $p<0.05$ were considered statistically significant.

Results

The three groups were well matched for age, body weight and surface area, pre-operative medication and baseline haemodynamic variables (Table 1). There was no significant difference between the three groups with respect to baseline HR, mean arterial pressure (MAP) or rate–pressure product (RPP) (Table 2).

There were small but nevertheless statistically significant rises in HR in all three groups at sternotomy ($p<0.01$). There was a highly significant rise in MAP at sternotomy in the control group ($p<0.001$), whilst in the ketanserin 10 mg group the rise was smaller and delayed until 90 seconds ($p<0.05$), and there was no significant rise in the ketanserin 20 mg group in immediate response to sternotomy. The highest pre-bypass MAP occurred at 6.7(3.5) minutes

Table 2. Haemodynamic data, mean (SD)

	Control	Ketanserin 10 mg	Ketanserin 20 mg
HR (beats/minute)			
Stage I	65(8.6)	64(8.6)	63(7.2)
Stage II	58(8.8)	55(5.7)	52(6.2)
Stage III	54(5.6)	55(7.0)	51(7.3)
Stage IV	60(7.1)†	59(6.2)†	57(7.7)†
Stage V	60(6.9)†	62(7.0)†	58(7.7)†
Stage VI	65(9.1)†	69(10.0)†	65(9.1)†
MAP (mmHg)			
Stage I	95(7.5)	95(13.7)	93(7.5)
Stage II	85(15.2)	81(8.4)	80(14.2)
Stage III	83(8.6)	94(14.4)	82(16.6)
Stage IV	100(10.1)†	89(13.0)	80(17.8)
Stage V	105(11.8)†	99(15.6)*	81(22.9)
Stage VI	113(9.6)†	124(24.3)†	97(22.3)*
RPP			
Stage I	8240(1630)	8300(1860)	7765(1020)
Stage II	6690(1560)	6080(1010)	5545(1120)
Stage III	6165(990)	6745(1625)	5540(1400)
Stage IV	8070(1295)†	6995(1415)	5915(1490)
Stage V	8670(1340)†	8060(1420)*	6130(1925)
Stage VI	10075(1740)†	11305(3150)†	8570(2630)†

Stage I: pre-op; stage II; stable anaesthesia; stage III: sternal incision; stage IV: sternotomy; stage V: 90 s post-IV; stage VI: highest value pre-bypass. *$p<0.05$ compared to stage III; †$p<0.01$ compared to stage III.

Table 3. Haematological data, mean (SD)

	Control	Ketanserin	
		10 mg	20 mg
Platelet count ($\times 10^9$/ml)			
Sample 1	0.240(0.04)	0.230(0.07)	0.210(0.07)
Sample 2	0.220(0.02)	0.220(0.06)	0.220(0.05)
Sample 3	0.230(0.02)	0.210(0.03)	0.210(0.04)
Platelet 5-HT (ng/10^9 platelets)			
Sample 1	522(219)	272(70)	434(95)
Sample 2	472(235)	310(121)	484(136)
Sample 3	463(239)	287(50)	471(126)
Plasma 5-HI (ng/ml)			
Sample 1	252(230)	197(57)	159(52)
Sample 2	217(56)	188(38)	169(39)
Sample 3	180(33)	188(44)	168(50)

Sample 1: stable anaesthesia; sample 2: sternal spread; sample 3: sternal spread + 10 minutes.
No significant difference at any stage.

post-sternotomy in the control group, at 10.7(5.4) minutes in the ketanserin 10 mg group and at 6.6(4.9) minutes in the ketanserin 20 mg group. The highest MAP recorded before bypass was significantly greater than at the commencement of surgery in all three groups ($p<0.001$). The changes in RPP reflected changes in HR and MAP (Table 2).

In the 13 patients in whom plasma 5-HI and platelet 5-HT levels were assayed, the first blood sample was taken 16.9(13.0) minutes prior to sternotomy, the second 4.6(1.2) minutes following administration of ketanserin or placebo and the third 14.6(1.3) minutes after injection. There was no significant difference in platelet count between the three groups before the commencement of bypass, and there were no significant changes in plasma 5-HI or platelet 5-HT levels in any of the three groups at any stage (Table 3).

Discussion

In the present study we administered two doses (10 mg or 20 mg) of ketanserin, a serotonin antagonist, intravenously, shortly before a standard surgical stimulus and compared with placebo the effect on HR and MAP. We found no difference in HR response, with all three groups exhibiting small but significant increases. The immediate rise in MAP in response to sternotomy was delayed by the lower dose of ketanserin and prevented by the higher dose. However, in all three groups, arterial blood pressure subsequently continued to rise before bypass. This rise was ameliorated but not entirely prevented by the higher dose of ketanserin. Rate-pressure product is considered to give some indication of myocardial oxygen demand,[19] and Kaplan has recommended that RPP should not be allowed to exceed 12000 in patients undergoing coronary artery surgery.[10] In the present study, RPP exceeded 12000 in six patients, but only in one patient in the high dose ketanserin group. We were unable to demonstrate any correlation between plasma or platelet serotonin levels and clinical response to ketanserin. Our results did, however, show a large degree of variability, which makes interpretation difficult.

Serotonin was first isolated in 1940 by Vittorio Erspamer and despite extensive research, its exact role in normal arterial blood pressure homeostasis remains speculative. Serotonin is found both peripherally and within the central nervous system. Peripherally, serotonin is synthesised from dietary tryptophan in the enterochromaffin cells of the gut. Serotonin overflowing from these cells enters the circulation and is metabolised by the liver and endothelial cells. Any serotonin escaping hepatic or pulmonary metabolism is avidly taken up by platelets and released during platelet aggregation or damage. Thus, platelets contain nearly all of the circulating serotonin, which is sequestered in specialised granules. Two distinct serotonin receptor sites have been proposed, S_1 and S_2. Binding of serotonin to the S_2 receptor correlates well with pharmacological effect of the amine. In healthy individuals, serotonin appears to play little part in the maintenance of cardiovascular homeostasis. However, in patients with atherosclerosis, specific increases in responsiveness of the blood vessel wall to the vasoconstrictor properties of serotonin may occur. In addition, serotonin enhances the vasoconstrictor properties of other agents such as the catecholamines. The hypertensive episodes seen in patients undergoing coronary artery surgery are known to be due to increases in peripheral vascular resistance rather than to increases in cardiac output. If serotonin does play a role in the maintenance of this augmented peripheral resistance, serotonergic antagonists may be expected to lower arterial blood pressure.

Ketanserin is a selective antagonist at the S_2 receptor in blood vessels, bronchial tissue and platelets, antagonising serotonin-induced vasoconstriction, bronchoconstriction and platelet aggregation. In addition, it has weak antihistaminic and anti-adrenergic activity and also inhibits the amplification by serotonin of vasoconstriction and platelet aggregation caused by other vaso-active agents such as adrenaline, noradrenaline and angiotensin II. Ketanserin has been previously shown to be effective in the treatment of per- and postoperative hypertension, including the hypertension following coronary artery surgery.[17,20] Although it is not yet clear whether the antivasoconstrictor effect is solely due to S_2 blockade, the possibility exists that ketanserin reduces blood pressure by a combination of S_2 receptor blockade and alpha-[1] adrenoceptor blockade.

In the present study, the platelet counts in all three groups were comparable but, despite this, the intraplatelet serotonin levels adjusted for platelet count were very variable within each group and showed no consistent change in response to sternotomy. The degree of within-group plasma 5-HI variability was similar to that found with the platelet 5-HT levels and again showed no consistent change in response to sternotomy. It should be pointed out that the spectrofluorimetric assay is not specific for 5-HT and will measure all 5-HI's present in the sample. Caution must therefore be exercised in the interpretation of the plasma values. However, it is thought that all of the contents of the platelet 5-HI stores is 5-HT, and the assay is thus accurate for intraplatelet serotonin. The values obtained for platelet serotonin are at the lower end of the normal range of 300–980 ng/10^9 platelets established by our laboratory, but the levels are in agreement with those of others[21-3] but they differed from those of Anger and Prys-Roberts.[24] It should be noted that the latter speculated that their sampling, preparation and handling techniques may have differed from those of previous workers. Conversely, the values obtained for plasma 5-Hs are in excess of the upper limit of the normal range of 0–160 ng/ml established by our laboratory.[23] The lack of correlation of platelet serotonin levels with ketanserin dose or clinical response strongly suggests that the effectiveness of the higher dose of ketanserin was due to an action at a site other than at the S_2 receptor. Anger, Carter, and Prys-Roberts,[25] by performing phenylephrine dose-response curves, demonstrated an anti-adrenergic action of ketanserin and this would certainly explain some of our findings. The observation of Ahtee and Saarnivaara[26] that certain narcotics, including pethidine and its derivatives (of which phenoperidine is one), can inhibit platelet uptake of 5-HT, may be an additional influencing factor.

In conclusion, this study demonstrated a dose-related effect of ketanserin in ameliorating the hypertensive response to sternotomy, but failed to show a clear correlation with plasma or platelet serotonin levels. The increased efficacy of the higher dose of ketanserin may be the result of blockade of the alpha-adrenoceptor rather than antagonism of serotonin.

Acknowledgments

We are grateful to Dr R.M. Jones for his advice and criticism in the preparation of this manuscript and to Janssen Pharmaceutical for providing us with the coded ampoules of ketanserin and placebo necessary for the study.

References

1. Viljoen JF, Estafanous FG, Tarazi RC. Acute hypertension immediately after coronary artery surgery. *Journal of Thoracic and Cardiovascular Surgery* 1976; **71**: 548–50.
2. Estafanous FG, Tarazi RC, Viljoen JF, El Tawil MY. Systemic hypertension following myocardial revascularization. *American Heart Journal* 1973; **85**: 732–8.
3. Fouad MF, Estafanous FG, Tarazi RC. Hemodynamics of postmyocardial revascularization hypertension. *American Journal of Cardiology* 1978; **41**: 564–9.
4. Feddersen K, Aurell M, Delin K, Häggendal J,

Arén C, Rådegran K. Effects of cardiopulmonary bypass and prostacyclin on plasma catecholamines, angiotension II and arginine–vasopressin. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 224–30.

5. Wilkinson PL, Hamilton WK, Moyers JR, Graham BG, Ports TA, Ullyot DJ, Chatterjee K. Halothane and morphine– nitrous oxide anaesthesia in patients undergoing coronary artery bypass surgery: patterns of intraoperative ischemia. *Journal of Thoracic and Cardiovascular Surgery* 1981; **82:** 372–82.
6. Edde R. Hemodynamic changes prior to and after sternotomy in patients anesthetized with high-dose fentanyl. *Anesthesiology* 1981; **55:** 444–6.
7. Roberts AJ, Niarchos AP, Subramanian VA, Abel RM, Herman SD, Sealey JE, Case DB, White RP, Johnson GA, Larragh JH, Gay WA. Systemic hypertension associated with coronary artery bypass surgery: predisposing factors, hemodynamic characteristics, humoral profile and treatment. *Journal of Thoracic and Cardiovascular Surgery* 1977; **74:** 846–59.
8. Wong KC, Martin WE, Hornbein TF, Freund FG, Everett J. The cardiovascular effects of morphine sulfate with oxygen and with nitrous oxide in man. *Anesthesiology* 1973; **38:** 542–9.
9. Lowenstein E, Philbin DM. Narcotic 'anesthesia' in the eighties. *Anesthesiology* 1981; **55:** 195–7.
10. Waller JL, Kaplan JA, Jones EL. Anesthesia for coronary revascularization. In: Kaplan JA, ed. *Cardiac Anesthesia.* New York: Grune and Stratton, 1979; 241–280.
11. Wallach R, Karp RB, Reves JG, Oparil S, Smith LR, James TN. Pathogenesis of paroxysmal hypertension developing during and after coronary bypass surgery: a study of hemodynamic and humoral factors. *American Journal of Cardiology* 1980; **46:** 559–65.
12. Stanley TH, Philbin DM, Coggins CH. Fentanyl–oxygen anaesthesia for coronary artery surgery: cardiovascular and anti-diuretic hormone responses. *Canadian Anaesthetists' Society Journal* 1974; **26:** 168–72.
13. Bailey DR, Miller ED, Kaplan JA, Rogers PW. The renin–angiotensin– aldosterone system during cardiac surgery with morphine–nitrous oxide anesthesia. *Anesthesiology* 1975; **42:** 538–44.
14. Townsend GE, Wynands JE, Whalley DG, Wong P, Bevan DR. Role of renin– angiotensin system in cardiopulmonary bypass hypertension. *Canadian Anaesthetists' Society Journal* 1984; **31:** 160–5.
15. Cashman JN, Jones RM, Thompson MA. Renin-angiotensin activation is not primarily responsible for the haemodynamic changes during sternotomy in patients undergoing cardiac surgery. *European Journal of Anaesthesiology* 1984; **1:** 299–303.
16. James TN, Isobe JH, Urthaler F. Analysis of components in a cardiogenic hypertensive chemoreflex. *Circulation* 1975; **52:** 179–92.
17. van der Starre PJA, Scheijgrond HW, Reneman RS, Kolling JB. The use of ketanserin, a 5-hydroxytryptamine receptor antagonist, for treatment of postoperative hypertension following coronary artery bypass surgery. *Anesthesia and Analgesia* 1983; **62:** 63–9.
18. Drummond AH, Gordon JL. Rapid, sensitive microassay for platelet 5-HT. *Thrombosis et Diathesis Haemorrhagica* 1974; **31:** 366–7.
19. Jones RM, Knight PR, Hill AB. Rate pressure product. *Anaesthesia* 1980; **35:** 1010–1.
20. Van Den Broeke JJW, Karliczek GF, Brenken U, Schokkenbroek R, Homan Van Der Heide JN. Is prevention of hypertension after open heart surgery possible by blocking 5-HT$_2$-receptors with ketanserin? *Acta Anaesthesiologica Belgica* 1982; **33:** 115–120.
21. Crawford N. Systemic venous platelet-bound and plasma free serotonin levels in non-carcinoid malignancy. *Clinica Chimica Acta* 1965; **12:** 274–81.
22. Shuttleworth RD, O'Brien JR. Intraplatelet serotonin and plasma 5-hydroxyindoles in health and disease. *Blood* 1981; **57:** 505–9.
23. Parbtani A, Frampton G, Cameron JS. Measurement of platelet release substances in glomerulonephritis: a comparison of beta-thromboglobulin (BTG), platelet factor 4 (PF 4) and serotonin assays. *Thrombosis Research* 1980; **19:** 177–89.
24. Anger C, Prys-Roberts C. Plasma serotonin during and after cardiac surgery. *European Journal of Anaesthesiology* 1984; **1:** 11–20.
25. Anger C, Carter J, Prys-Roberts C. Ketanserin and postoperative hypertension following cardiopulmonary bypass. *British Journal of Anaesthesia* 1984; **57:** 339P.
26. Ahtee L, Saarnivaara L. The effect of narcotic analgesics on the uptake of 5-hydroxytryptamine and (-)-metaraminol by blood platelets. *British Journal of Pharmacology* 1973; **47:** 808–18.

Anaesthesia, 1986, Volume 41, pages 511–515

CASE REPORT

Ventricular volume and ejection fraction in the diagnosis of the aetiology of low cardiac output in burned patients

J. A. J. MARTYN, K. MCKUSICK, H. W. STRAUSS AND J. F. BURKE

Summary

Cardiovascular instability following burns may result from either cardiac or non-cardiac causes. We illustrate three cases in whom routine measurements of atrial filling pressures and cardiac output alone did not reflect the adequacy of blood volume or the myocardial performance. In each instance, measurements of ventricular volume and ejection fraction by thermodilution technique or ^{99m}*TC ventriculography were useful to determine the actual causes of decreased cardiac output.*

Key words
Heart; output, ventricles.
Intensive care.

Cardiac instability in burned patients can result from hypovolaemia, burn-induced direct myocardial depression, or sepsis.[1] The secondary effects of therapy with positive end expiratory pressure (PEEP)[2] and drugs, particularly anaesthetics[3] can further aggravate cardiovascular instability. Measures most commonly used to assess the adequacy of cardiovascular function, i.e., urine output, central venous (CVP) and pulmonary capillary wedge pressures (PWP), and cardiac index (CI) may be inadequate in certain critically ill patients.[4] For example, assessment of cardiac function by filling pressures can be misleading when airway pressure is increased, as with PEEP[2] or when ventricular compliance is altered because of hypertrophy, pericardial effusion, or drugs.[3-5] Under these circumstances, increased filling pressures can be found in the presence of hypovolaemia and normal myocardial contractility. This can lead to an erroneous conclusion about the cause of the cardiovascular instability.

Ventricular volume and ejection fraction can be monitored at the bedside of critically ill patients by the thermodilution technique,[4,5] or by gated blood pool imaging,[6] and can enhance the assessment of cardiovascular function. While the former technique requires the modification of the flow directed pulmonary artery (PA) catheter, the latter technique requires the assistance and expertise of the radiologists. The accuracy and reproducibility of these measurements has been confirmed.[6,7,8] We describe three clinical cases in whom filling

---

J.A.J. Martyn, MD, FFARCS; Associate Professor of Anaesthesia, Harvard Medical School, Massachusetts General Hospital and Associate Director of Anaesthesia, Shriner's Burns Institute, Boston, Massachusetts 02114, U.S.A., K. McKusick, MD, Associate Professor of Radiology, Harvard Medical School and Clinical Director, Division of Nuclear Medicine, Massachusetts General Hospital, Boston, Massachusetts 02114, U.S.A., H.W. Strauss, MD, Professor of Radiology, Harvard Medical School and Director, Division of Nuclear Medicine, Massachusetts General Hospital, Boston, Massachusetts 02114, U.S.A., J.F. Burke, MD, Professor of Surgery, Harvard Medical School and Chief of Trauma Services, Massachusetts General Hospital, Boston, Massachusetts 02114, U.S.A.

0003–2409/86/050511 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

pressures and CI measurements alone were misleading in the assessment of cardiac function, while knowledge of ventricular volumes and ejection fraction by either method helped identify the cause of reduced cardiac output.

Methods

The technique of thermodilution right ventricular volume (RVV) measurements has been described previously.[4,5] The proximal port of the triple lumen, flow-directed PA catheter was modified to allow the injection of iced saline directly into the right ventricle (RV) instead of the right atrium. The washout of cold saline from the RV was detected in the PA by a rapid sensing thermistor. The downslope of the thermal washout curve was characterised by a series of successive diastolic plateaux, corresponding to cardiac ejection. The ratio of the end-diastolic plateaux was used of calculate RVV$_{\mathrm{TD}}$ and RVEF$_{\mathrm{TD}}$.[4,5] The normal mean (SD) of RVV$_{\mathrm{TD}}$ and RVEF$_{\mathrm{TD}}$ are 98 (SD 23) ml/sq m and 0.43 (SD 0.05) respectively.

Radionucleide ventriculography was performed following a bolus injection of 740 millibecquerels (= 20 millicurie) of technetium -99m (^{99m}TC) labelled red blood cells, labelled using a modified method of Callahan *et al.*[9] Using a *mobile* scintillation camera, equipped with an all-purpose parallel hole collimator and interfaced to a computer (Technicare 550), all data were collected in a 64 × 64 format at a minimum of 16 frames/cardiac cycle. The ^{99m}TC right ventricular ejection fraction (RVV$_{\mathrm{TC}}$) was calculated from a first pass gated acquisition in a 30° right anterior oblique projection;[6] a normal ejection fraction using this technique would be 0.6 (SD 0.07). Gated equilibrium data were obtained from anterior and left anterior oblique projections, with a count density of 250 over the left ventricle.

Case histories

Case 1: Pericardial tamponade confused with heart failure

A 45-year-old male developed myoglobinaemic renal failure following severe electrical injury and was on haemodialysis. About 40 days after the burn, he developed gradual respiratory distress and required mechanical ventilation with PEEP. Chest X ray revealed massive cardiomegaly with bilateral pulmonary oedema. On the 52nd day after the burn, he suddenly became hypotensive, requiring dopamine to maintain his systemic blood pressure. A modified PA catheter[4,5] and an intra-arterial cannula were inserted. His temperature was 36.7°C, and blood pressure and heart rate on 400 μg/minute of dopamine were 130/73 mmHg and 83 beats/minute respectively. On $F\mathrm{io}_2$ 0.4 with mechanical ventilation and 0.5 kPa PEEP, the arterial and mixed venous blood gases were $P\mathrm{ao}_2$ 13.7 kPa, $P\mathrm{aco}_2$ 5.7 kPa, pH 7.32 and $P\bar{\mathrm{v}}\mathrm{o}_2$ 6.7 kPa, $P\bar{\mathrm{v}}\mathrm{co}_2$ 6.3 kPa, pH 7.29. The PA pressure was 40/26, with a PWP and CVP of 22 and 23 mmHg, respectively. The CI was 2.8 l/minute/sq m. Analysis of RV end-diastolic pressure, PA diastolic pressure, and PWP contours to detect cardiac tamponade was difficult because of marked fluctuations in these pressures with ventilation. The high PWP and relatively low CI for a burned patient were suggestive of global cardiac failure.

The RVV$_{\mathrm{TD}}$, however, was normal (78 ml/sq m) and RVEF$_{\mathrm{TD}}$ high normal (0.64), [normal RVV$_{\mathrm{TD}}$ = 98 (SD 23) ml/sq m and RVEF$_{\mathrm{TD}}$ = 0.43 (SD 0.5)].[5] Thus, the finding of a normal RV volume with high RVEF was incompatible with a diagnosis of heart failure. A technically difficult echocardiogram suggested posterior pericardial and left pleural effusions. Because the echo study was inconclusive, a ^{99m}TC radionucleide ventriculogram was obtained. The right heart first pass study showed a normal-sized right ventricle and no reflux with an RVEE$_{\mathrm{TC}}$ of 0.66. The left ventricular ejection fraction by ^{99m}TC was (LVEF$_{\mathrm{TC}}$) elevated at 0.78 and the left ventricle end-diastolic volume was small. A massive photon deficient area surrounded the heart, indicative of massive pericardial effusion. Findings suggestive of bilateral pleural effusion were also present. (The pericardial and pleural fluid cannot freely mix with radiolabelled red cells and therefore do not become photon emitters; these therefore appear as photon deficient areas.)

On the basis of these results, a diagnosis was made of pericardial tamponade with bilateral pulmonary effusions due to increased hydrostatic pressure of the left ventricle and uraemia. At pericardiocentesis, 600 ml of serosanguineous fluid were withdrawn. Immediately after pericardiocentesis, CVP and PWP decreased to 10–15 mmHg, and CI improved to 3.3 l/minute/sq m, confirming that the decreased CI and increased filling pressures were due to cardiac tamponade. The patient was discharged to a hospital closer to his home for continued haemodialysis.

Case 2: Cardiac failure and permeability pulmonary oedema

A 35-year-old female sustained an 80 percent burn with severe inhalation injury. On the third day after the burn, she was hypertensive and in severe respiratory failure, requiring an $F\mathrm{IO}_2$ 0.6 and PEEP of 1.5 kPa to maintain $P\mathrm{aO}_2$ over 9.3 kPa. Chest X ray revealed bilateral pulmonary oedema. In addition, she was oliguric and had a positive toluidine test for myoglobinaemia. Blood urea nitrogen was 17 mmol/litre urea and serum creatinine was 304 μmol/litre. Low dose dopamine (100 μg) did not significantly improve her urine output. Systematic arterial and central venous pressures were 185/86 and 14 mmHg, respectively, and the heart rate was 140 beats/minute. Because she was dependent on PEEP, CVP could not be measured at zero PEEP, so it was impossible to determine the contribution of increased airway pressure to the measured increase in CVP. Because of the timing of the injury, pulmonary oedema could have been caused by volume overload resulting from fluid mobilisation, particularly in the absence of renal function, or by inhalation injury. Following insertion of a modified PA catheter, the CI was measured to be 3.44 l/minute/sq m, the PA pressure 24/14 mmHg, and PWP 15 mmHg. Calculation of $\mathrm{RVV_{TD}}$ showed a low volume (58 ml/sq m) and $\mathrm{RVEF_{TD}}$ of 0.55. Radionucleide ventriculography showed the ejection fractions to be 0.63 with low biventricular volumes.

The increased biventricular ejection fractions with low ventricular volumes suggested the presence of volume depletion. Thus, pulmonary oedema was not due to left ventricular failure, but was caused by inhalation injury. The PWP was maintained at about 15 mmHg and renal function was facilitated by peritoneal dialysis and low dose dopamine. Hypertension, even in the presence of hypovolaemia, is not uncommon and is probably caused by humoral factors. Eventually, this patient's renal and pulmonary function returned to normal and she was discharged home following healing of the burn wound.

Case 3: Differentiation of isolated right ventricular from biventricular failure

An 81-year-old male had sustained a 30 percent burn in a house fire. The patient was on digoxin for a past history of congestive heart failure and had chronic renal failure with a creatinine of 152 μ mol/litre. On the ninth day after the burn, he was in a respiratory failure, requiring mechanical ventilation with 2.0 kPa PEEP and $F\mathrm{IO}_2$ 0.6. Chest X ray showed a very enlarged heart with bilateral pulmonary oedema. The heart rate was 88 beats/minute. The systemic and PA pressures were 108/70 and 60/30 mmHg respectively, with a PWP and CVP of 22 and 18 mmHg respectively. The arterial and venous blood gases were $P\mathrm{aO}_2$ 13.7 kPa, $P\mathrm{aCO}_2$ 5.5 kPa, pH 7.44 and $P\bar{\mathrm{v}}\mathrm{O}_2$ 4.9 kPa, $P\bar{\mathrm{v}}\mathrm{CO}_2$ 6.1 kPa, and pH 7.41. The CI was 2.01/minute/sq m with a $\mathrm{RVV_{TD}}$ of 141 ml/sq m and $\mathrm{RVEF_{TD}}$ of 0.15. It was unclear how much of the increased PWP and low CI was due to increased airway pressure (PEEP).[2] The possibility of an enlarged right ventricle as a cause for the rise in PWP was considered: an enlarged right ventricle can encroach on the left ventricular wall, altering pressure–volume relationships.[5]

An radionuclide ventriculogram showed biventricular dilation with global hypokinesis. The $\mathrm{LVEF_{TC}}$ was 0.18 and the $\mathrm{RVEF_{TC}}$ 0.16, indicating biventricular global dysfunction. The patient was started on dopamine, while the CI and $\mathrm{RVEF_{TD}}$ were monitored. The dose of dopamine was gradually increased until the CI and $\mathrm{RVEF_{TD}}$ stabilised at 3.21/minute/sq m and 0.22 respectively at a dopamine infusion rate of 600 μg/minute. A few days later, however, he developed a myocardial infarction and died.

Discussion

The classical measurements of cardiac function, namely atrial filling pressures and cardiac and urine output, are not always reliable in distinguishing between inadequate blood (circulating) volume and inadequate myocardial function as the causes of low cardiac output in burned patients. In Case 1, although the clinical evidence suggested pericardial effusion, a definitive diagnosis was made only after radionuclide ventriculography. Thus, in the first case, the increased atrial filling pressure was caused by elevated pericardial and pleural pressures. In Case 2, the findings of systemic hypertension, elevated PWP and bilateral pulmonary oedema suggested volume overload. However, because of the associated renal dysfunction, it was important to determine whether the cause of the patient's oliguria was prerenal. This patient was extremely PEEP-dependent, so the assessment of volume status (preload) and myocardial function by filling pressures and CI was impossible. Therefore, an estimate of the ventricular volume and ejection fraction was obtained. Since the ventricular volumes were small and the contractions hyperdynamic, we concluded that the pulmonary oedema was due to the increased permeability of inhalation injury, not left ventricular failure due to volume overload. An intense sympathetic response might explain the hyperdynamic biventricular function observed in this patient.

The massive cardiomegaly and PWP of 22 mmHg in Case 3 were compatible with both pericardial effusion and heart failure. Because there was no equalisation of PWP and CVP, pericardial effusion was unlikely. Ventriculography confirmed the diagnosis of heart failure. Repeated bedside thermodilution measurements of ventricular volume and ejection fraction were useful in monitoring cardiovascular response to increasing doses of dopamine.

Cardiac function is dependent on filling volume, contractile state and resistance to ejection of the ventricle. Certain assumptions are made when using PWP as a guide to blood volume and ventricular function, namely PWP = left atrial pressure, left atrial pressure = left ventricular end diastolic pressure, and left ventricular end diastolic pressure = K (a constant) × left ventricular and diastolic volume. These assumptions may not apply in certain critically ill patients, when there is an increased intrathoracic pressure (as with PEEP) in valvular heart disease, or when the compliance of the ventricle is changed as a consequence of hypertrophy, disease, or drugs.[3,5] Therefore, serious errors in judging ventricular performance can occur when filling pressures are used, even in combination with CI. The studies of Shah *et al.*[12] and Martyn *et al.*,[4] in which a poor correlation was shown between PWP and CI, are consistent with this view. Thus, as illustrated in these three cases, in certain clinical situations, inappropriate therapy may result if one uses PWP and/or CI as a guide to blood volume or ventricular function. On the other hand, ventricular volume and ejection fraction measured by thermodilution or ^{99m}TC provide useful information on both volume and global and regional contraction of the myocardium. These latter tools not only aid in the diagnosis, but help one to assess and to monitor the efficacy of therapeutic intervention.

The principle of the indicator dilution technique for the measurement of ventricular volume and ejection fraction has been described previously.[13] Making use of this principle, we modified the conventional PA catheter in order to measure both RVV and RVEF by thermodilution.[4,5] Recent studies have compared $RVEF_{TD}$ and $RVEF_{TC}$, and found a correlation ($r = 0.86$) between the two techniques[7,8]. In cases 1 and 3, the $RVEF_{TD}$ was very close to the $RVEF_{TC}$ and in Case 2, the marked tachycardia may have contributed to the small discrepancy. At pulse rates of over 140 beats/minute, the response time of the thermistor may have been at the upper limit of its range, causing the discrepancy.

There are several advantages to using thermodilution for the measurement of RV volume and ejection fraction. It is a bedside procedure, it can be performed repeatedly without limitation and it is simple to calculate. Thus, it is useful not only in diagnosing the aetiology of cardiovascular instability, but also assessing the efficacy of therapy. Unfortunately, this technique does not enable the evaluation of left ventricular function. The appeal of the gated blood pool scan is that it is non-invasive, carries negligible risk for the patient and yields information about both right and left ventricles. Furthermore, it can be performed at the bedside even in the most sick patients, providing information on global as well as regional function that previously has been difficult, if not impossible, to obtain by contrast angiography. Echocardiography was attempted in two patients. However, insufficient information was derived from this procedure because of technical difficulties inherent in the burn patient, (e.g. dressings).

In conclusion, these three cases illustrate that the measurement of ventricular volume and ejection fraction either by thermodilution or by ventriculography may provide additional, useful tools for the management of critically ill patients, giving more accurate estimates of the filling and contractile state of the heart.

Acknowledgments

Supported in part by a grant from Shriner's Burns Institute and from the NIH GM21700 and 31569.

References

1. Moncrief JA. Burns. *New England Journal of Medicine* 1973; **288:** 444–54.
2. Qvist J, Pontopiddan H, Wilson RS, Lowenstein E, Laver MB. Hemodynamic responses to mechanical ventilation with PEEP: The effect of hypervolemia. *Anesthesiology* 1975; **42:** 45–55.
3. Hamilton WK, Larson CP, Bristow JD, Rappaport E. Effects of cyclopropane and halothane on ventricular mechanisms: a change in ventricular pressure–volume relationships. *Journal of Pharmacology and Experimental Therapeutics* 1966; **54:** 566–74.
4. Martyn JAJ, Snider MT, Farago LS, Burke JF. Thermodilution right ventricular volume, a novel and better predictor of volume resuscitation in burned patients. *Journal of Trauma* 1981; **8:** 619–26.
5. Martyn JAJ, Snider MT, Szyfelbein SK, Burke JJ, Laver MB. Right ventricular dysfunction following acute thermal injury. *Annals of Surgery* 1980; **191:** 330–335.
6. Winzelberg GG, Boucher CA, Pohost GM, McKusick KA, Bingham JB, Okada RD, Strauss HW. Right ventricular function in aortic and mitral valve disease. *Chest* 1981; **79:** 520–8.
7. Byrnjolf I, Qvist J, Mygind T, Jordening H, Dorph S, Munck O. Measurement of right and left ventricular ejection fraction in dogs. *Clinical Physiology* 1983; **3:** 335–48.
8. Kay M, Afshari M, Barash P, Webler W, Iskandian A, Bemis C, Hadi Jai A, Mundth ED. Measurement of ejection fraction by thermodilution techniques. *Journal of Surgical Research* 1983; **34:** 337–46.
9. Callahan RJ, Froelich JW, McKusick KA, Leppo J, Strauss HW. A modified method for the *in-vivo* labeling of red blood cells with Tc-99m: Concise communication. *Journal of Nuclear Medicine* 1982; **23:** 315–8.
10. Moran RJ, Martyn JAJ, Philbin DM, Coggins CM, Burke JF. Water metabolism and antidiuretic hormone response following thermal injury. *Journal of Trauma* **10:** 468–72.
11. Akrami C, Falkner B, Gould AB, DeClement FA, Bendlin A. Plasma renin and occurrence of hypertension in children. *Journal of Trauma* 1980; 130–4.
12. Shah DM, Browner BD, Dutton RE, Newell JC, Powers SR. Cardiac output and pulmonary capillary wedge pressure. *Archives of Surgery* 1977; **112:** 1161–8.
13. Holt JP. Estimation of residual volume of dog's heart by two indicator dilution techniques. *Circulation Research* 1965; **4:** 187–94.
14. Rolett EL, Sherman H, Gorlin R. Measurement of left ventricular volume of thermodilution: an appraisal of technical errors. *Journal of Applied Physiology* 1964; **19:** 1164–74.

Anaesthesia, 1986, Volume 41, pages 516–518

APPARATUS

A portable oxygen generator

L. W. HALL, R. E. B. KELLAGHER AND K. J. FLEET

Summary

The use of a portable generator which liberates oxygen from hydrogen peroxide solutions has been investigated in veterinary anaesthesia to assess its potential as an alternative to conventional oxygen supplies both in emergency situations and in the event of failure of cylinder systems. The reliability of the supply appears to be good and the operation of the generator simple, making it suitable for a number of potential uses. It should compare favourably with oxygen concentrator devices used for similar purposes.

Key words

Oxygen; preparation, delivery systems.

There are circumstances where obtaining oxygen from heavy, bulky containers is inconvenient or impossible and for many years there has been considerable interest in alternative sources of supply.[1] More recently, interest has been revived because of the special needs of the developing countries[2] and military campaigns.[3] The oxygen concentrator using a molecular sieve of zeolite has been developed to meet these needs, but unreliability may have limited its widespread use,[4] although there are indications that these machines have improved.[5] An oxygen generator system requiring only electrical power and hydrogen peroxide solution as fuel may provide an alternative, reliable, source of oxygen for many applications. This paper describes the principles of operation, specification and performance of a portable oxygen generator which has undergone preliminary trials in veterinary anaesthesia and its potential application in other fields is discussed.

Principle of operation

The principle on which this oxygen generator works has been known for a very long time. A solution of hydrogen peroxide 'fuel' is dissociated into oxygen and water, accompanied by an exothermic reaction according to the equation

$$H_2O_2 \rightarrow H_2O + 1/2\ O_2 + 98\ \text{kJ/mole}\ H_2O_2$$

Johnson Matthey Chemicals Ltd., Equipment Division (JMC) have recently produced an oxygen generator which uses a precious metal catalyst to promote the dissociation of the fuel. A control mechanism[6] regulates fuel consumption and liberates oxygen at a set pressure of 28 kPa. If oxygen consumption ceases or produc-

---

L.W. Hall, PhD, DVA, MRCVS, Reader in Comparative Anaesthesia, R.E.B. Kellagher, BVSc, MRCVS, DVA, University Assistant Anaesthetist, University of Cambridge, Department of Clinical Veterinary Medicine, Madingley Road, Cambridge CB3 0ES, K.J. Fleet, BSc, Engineering, Principal Development Engineer, Johnson Matthey Chemicals Ltd., South Way, Exhibition Grounds, Wembley HA9 0HW.

0003–2409/86/050516 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

tion exceeds usage, the fuel supply automatically stops when the oxygen pressure reaches 56 kPa; a further safety valve is incorporated at 84 kPa. Oxygen consumption restarts the flow of fuel to the reaction chamber. As the release of oxygen is exothermic, the generated gas has to be cooled. To dissipate the heat by use of cooling fins or any form of heat-exchanger, using natural draught cooling, would add greatly to the complexity, bulk and weight of the apparatus. For these reasons, the generator is cooled by a forced draught system provided by a low-powered, electrically-driven fan. Pure oxygen mixed with water vapour is generated and although drying of the gas only presents problems at flows of above about 5 litres/minute, a molecular sieve is used to dry it before it passes through any flowmeter.

The strong (35 percent w/w) technical grade solution of hydrogen peroxide used as fuel yields 130 litres of oxygen/litre of solution. It is very widely used as a bleaching agent and in pulping processes and is obtainable throughout the world. This fuel is safe to handle in bulk and is easily transported, preferably in containers which do not need to be returnable. It can be most unpleasant if splashed on the skin or into the eyes and ways of filling the fuel tank which do not carry the risk of such splashing entail the use of closed containers and a suitably designed filling system.

For oxygen enrichment of air used in drawover anaesthetic systems, a 500-ml capacity reservoir tube is incorporated with an isolator valve inside the casing of the generator (Fig. 1).

Purity of the oxygen and composition of waste products

Analysis of the oxygen delivered from the generator indicates that it is more than 99 percent (v/v) pure and thus should meet the standards for oxygen BP. The waste product from the generator is water which, while not pure, contains only the stabilisers from the technical grade hydrogen peroxide. These impart a faint smell to the waste water but they are non-toxic.

Operation of the generator

The preparation of the apparatus for use is extremely simple. The oxygen drier is checked and if the indicator incorporated in the molecular sieve indicates that its absorbent capacity is exhausted the sieve is changed. (This has not proved to be necessary in over 200 hours of use). The level of fuel in the tank is observed and the tank is replenished as required. The water level in the waste tank is noted, any present is drained off and the apparatus is connected to a source of electrical power. Switching on the power opens the fuel solenoid valve, oxygen generation starts and an adequate supply pressure is achieved within a few seconds. An audible signal sounds until the operating pressure is reached and when this ceases oxygen flows of up to 5 litres/minute may be drawn off. The audible warning may also sound when the fuel level is too low, or if the water level is too high. Waste water can be drained from the apparatus at any time while oxygen is being generated, but replenishing the fuel tank is only possible by temporarily interrupting the oxygen supply. To stop operation the power is switched off and the oxygen flow control turned off once the system has vented.

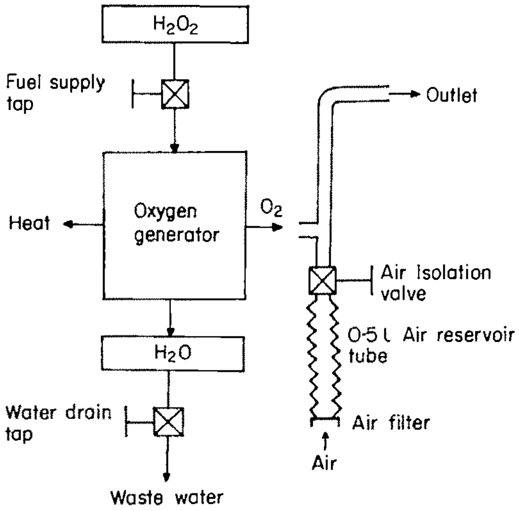


Fig. 1. Diagram showing the main components of the oxygen generator system.

Trials in veterinary anaesthesia

Oxygen from the apparatus has been used to enrich air in a drawover system, as the total gas flow in T-piece systems and to volatilize agents from vaporizers placed outside the breathing system for low-flow absorption techniques. In the drawover system using an Oxford Miniature vaporizer, self-inflating bag and Ambu non-rebreathing valve, an oxygen flow of 1 litre/

minute has provided sufficient enrichment of the air to guarantee very satisfactory oxygenation in spontaneously breathing dogs of over 15 kg bodyweight. Arterial oxygen tension has never been found to be less than 26 kPa. At a flow of 1 litre/minute, one fuel tank of peroxide provided some 5.5–6 hours supply of oxygen. Using a T-piece system with flows of up to 2 litres/minute for cats and small dogs, one tank full of fuel was sufficient for about 2.5 hours of anaesthesia.

The apparatus proved to be both reliable and trouble-free. In providing more than 200 hours of anaesthesia, it required no attention other than draining of the waste water and filling the fuel tank; care had to be taken to avoid splashing the strong hydrogen peroxide on to the skin, clothing or into the eyes.

Potential use

The JMC portable oxygen generator was designed particularly for use in veterinary anaesthesia but other applications can be readily envisaged. In domiciliary practice its use would eliminate the problems associated with cylinder changing and supply in long term oxygen therapy. It is also simpler to operate and less hazardous than systems using pressurised cylinders. The generator could be used extensively by the medical services of the armed forces (and might well have been extremely valuable in the Falklands campaign), since the transport of the hydrogen peroxide in tanks or disposable containers is a simple, relatively safe procedure compared with the transport of compressed gases. An oxygen generator is a potential source of oxygen in rescue helicopters, ambulances and at major disasters.

The apparatus is easily transported and light enough to be carried by an ordinary man or woman for relatively long distances. Although all the prototype generators have run off the mains supply of electricity or from a car battery, the cooling fan does not require much power and there is no reason why the unit could not function for many hours running off a small rechargeable battery or a battery pack. Even the fuel could be transported in the fuel tank and thus, on an emergency call, all that need be taken would be the apparatus itself with a breathing system and, for inhalation anaesthesia, a vaporizer.

In more sophisticated centres it could provide oxygen supplies to areas without a pipeline system supply or during pipeline servicing. Scaling up and deliveries of hydrogen peroxide by bulk tanker may provide an oxygen source for pipeline systems for the oxygen supply pressure can be increased. In use, the oxygen generator using hydrogen peroxide as a source of oxygen seems to compare favourably with the oxygen concentrator. The oxygen concentrator has the disadvantage of requiring maintenance and the people most likely to need the oxygen would seem to be those most unlikely to be capable, or willing, to attend to this essential matter. The oxygen generator needs very little attention—the only moving part is the cooling fan and this should need no more attention than an ordinary domestic kitchen extractor fan.

Conclusions

The JMC oxygen generator appears to be capable of providing oxygen enrichment of air for draw-over anaesthetic systems, or pure oxygen for other applications, in a reliable manner whenever and wherever supplies of hydrogen peroxide and electrical power are available. It requires the minimum of maintenance and is very simple to operate.

References

1. Cotes JE, Douglas-Jones AG, Saunders MJ. A 60% oxygen supply for medical use. *British Medical Journal* 1969; **4:** 143–6.
2. Ezi-Ashi TI, Papworth DOP, Nunn JF. Inhalational anaesthesia in developing countries. Part 1: The problem and the proposed solution. *Anaesthesia* 1983; **38:** 736–47.
3. Bull PT, Merrill SB, Moody RA, Baker DJ, Yates A, Geraghty F, Tighe SQM, Squires SJ, Stoot CJ. Anaesthesia during the Falklands campaign. The experience of the Royal Navy. *Anaesthesia* 1983; **38:** 770–6.
4. Evans TW, Waterhouse J, Howard P. Clinical experience with the oxygen concentrator. *British Medical Journal* 1983; **3:** 459–61.
5. Carter JA, Baskett PJF, Simpson PJ. The 'Permox' oxygen concentrator. *Anaesthesia* 1985; **40:** 560–565.
6. Fleet KJ. Generation of gas and control regulator for use therein. Patent Application No. GB84/29304.

Anaesthesia, 1986, Volume 41, pages 519–526

APPARATUS

Selective bronchial intubation for one lung anaesthesia in thoracic surgery

A new method

S. NAZARI, R. TRAZZI, F. MONCALVO, A. ZONTA AND M. CAMPANI

Summary

A new method for one lung anaesthesia in thoracic surgery is described. Separate lung ventilation is obtained with selective main bronchus intubation, by means of an appropriate cuffed tube inserted through a standard orotracheal tube. Ventilation is carried out separately through the bronchial tube on one side and the residual tracheal tube lumen on the other side. This method greatly simplifies the technique of bronchial intubation and offers many advantages over commercially available double-lumen tubes.

Key words

Equipment; tubes, bronchial.
Anaesthesia; thoracic.

Anaesthesia in thoracic surgery is commonly carried out with the aid of double-lumen tracheobronchial tubes,[1-12] in order to obtain selective exclusion of one lung. Separate ventilation has several important purposes: to prevent postural contralateral bronchial flooding with blood and/or secretions from the manipulated lung in the operative field, to allow 'open bronchus' surgery and to make surgical manoeuvres on the operative field easier by collapsing or inflating the exposed lung.

Commercially available double-lumen tubes actually allow separation of the two lungs but occasionally they are difficult to position and serious complications have been reported.[4,13-15] The purpose of this paper is to describe a new method for selective bronchial intubation recently set up in our department and evaluated in patients undergoing pneumonectomy for lung cancer.

Apparatus and methods

Separate ventilation is achieved by means of an appropriate cuffed bronchial tube, whose tip is positioned in a main bronchus by passing it through a standard orotracheal tube (Fig. 1). The tubes assembled in this way make up two independent channels (Fig. 2) each in communication with one of the main bronchi. Ventilation is then carried out separately through the bronchial tube on one side and the residual tracheal tube lumen on the other side.

Figure 2 shows a schematic section of the bronchial and tracheal tubes assembled for use. The bronchial tube is not exactly co-axial to the

---

S. Nazari, MD, Sezione di Patologia Chirurgica, Dipartimento di Chirurgia, Università di Pavia, R. Trazzi, MD, Direttore II Cattedra di Anestesia e Rianimazione dell'Università di Milano, F. Moncalvo, MD, Direttore della Divisione di Pneumologia, Istituto di Ricovero e Cura a Carattere Scientifico, Policlinco S. Matteo, Pavia, A. Zonta, MD, Direttore del Dipartimento di Chirurgia della Università di Pavia, M. Campani, MD, Direttore della Sezione di Patologia Chirurgica del Dipartimento di Chirurgia della Università di Pavia, 27100, Pavia, Italy.

0003–2409/86/050519 + 08 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

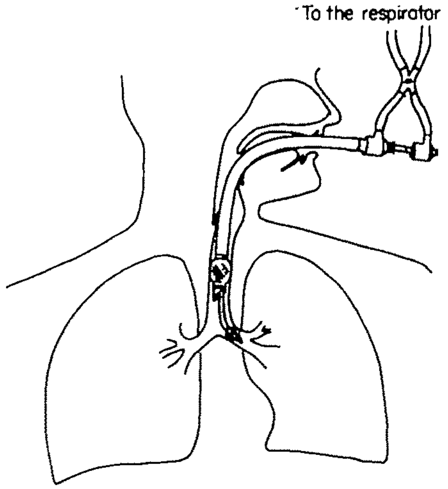


Fig. 1. Schematic representation of the positioned device. A Y-shaped pipe connects the two channels to the ventilator.

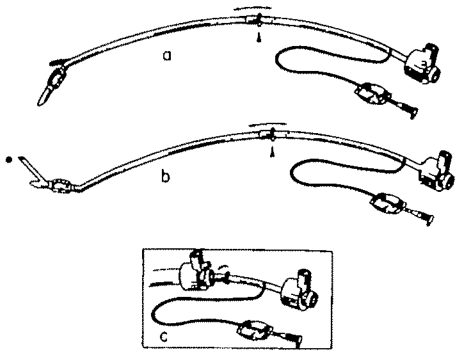


Fig. 3. The bronchial tubes for intubation of the left (a) and the right (b) main bronchus (●), the lateral branch will be engaged in the right upper lobe bronchus. Thus, advancement of the tube will stop before its cuff obstructs the origin of the upper lobe bronchus (see intubation technique). (▲), Movable ring for the external airtight connection between the two tubes. (c), External connexion between the two tubes.

tracheal tube, but can move freely in the main lumen; nevertheless, the total section of the outer channel is always constant. The size of the tubes are such that they supply two channels with similar air flow resistance; this allows the anaesthetic gases to be delivered through a Y-shaped pipe connected to both channels, supplying the same flow in the two lungs when they are both being ventilated.

Figure 3 shows the bronchial tubes for right and left main bronchus intubation*. Both tubes are fitted with a movable plastic ring (Fig. 3) that allows variable reciprocal positioning of the two tubes and acts as an external airtight connexion. An opening in the connector allows the introduction of a small suction catheter in the outer tracheal channel (Fig. 2C). The distal end of the right bronchial tube is fitted with a side branch originating immediately after the cuff, forming a 45° angle with the major axis of the tube (Fig. 3b). When the tube is in place, this branch engages in the right upper lobe bronchus; in this way, advancement of the tube is stopped before its inflated cuff obstructs the origin of the right upper lobe bronchus (see intubation technique).

Two sets of tubes were manufactured and tested. The first set was associated with a low resistance to gas flow. It consisted of a standard 10 mm ID tracheal tube (external diameter 14 mm) and a cuffed tube of 5.5 mm ID and 7.4 mm external diameter for selective bronchial intubation. The second set had a higher resistance to gas flow and consisted of a 9 mm ID standard tracheal tube and a 5 mm ID, 6.8 mm external diameter, cuffed tube for bronchial intubation.

The resistance to flow in the whole isolated system as well as in each of the two channels separately was determined with an Engström

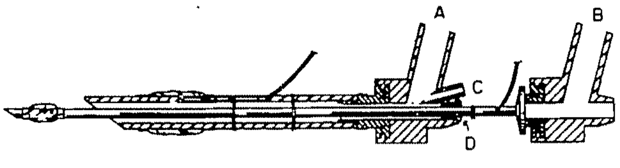


Fig. 2. Schematic section of the two tubes assembled for use. (A) and (B) the connectors for ventilation of the tracheal and bronchial channels. (C) the entrance for the suction catheter of the tracheal channel. (D) movable ring for the external airtight connexion between the tubes.

---

*Bronchial tubes are available from Pusic, P.O. Box 99, 27100 Pavia, Italy.

ventilator system model 300 ER 321 and a Medishield RM 121 spirometer. This technique of bronchial intubation has been used in 21 patients undergoing pneumonectomy for lung cancer (7 right, 14 left).

Intubation technique

Although the tubes can be positioned in several ways, our own experience suggests the following technique. The tracheal tube is inserted deep into the trachea using the standard technique; its inner surface is adequately lubricated with vaseline. After ventilation of the lungs, the lubricated and properly oriented bronchial tube (Fig. 4) is inserted into the main tracheal tube and advanced as in Fig. 4a.

A special mark on the bronchial tube denotes that the tip of the tube and its cuff have emerged from the tracheal tube (Fig. 4b). For right bronchus intubation, the properly orientated tube is again pushed down for a further few cm, until an increase in resistance indicates that the correct position has been reached, with engagement of the lateral branch in the right upper lobe. In this way bronchial tube advancement is stopped before its cuff obstructs the origin of the upper right lobar bronchus.

The bronchial tube usually enters the right main bronchus with no need for guidance, due to its less acute angulation from the tracheal axis. To intubate the left main bronchus, when the tip of the bronchial tube has reached the trachea, a guide is inserted (Fig 5a). The tube is then pushed down, properly orientated, for a few cm (Fig. 5b) and the guide withdrawn (Fig. 5c). The tubes are then fixed with the external movable plastic ring, which firmly maintains the position of the bronchial tube (Fig. 3c). The site of the bronchial tube can be checked by directly testing the effects of alternate selective exclusion of each of the tubes on the lungs by the usual methods (auscultation, measurement of exhaled air flow, etc.).

Bronchial intubation may also be carried out during surgery, when the patient is in the lateral decubitus position. In this event, the proper positioning of the tube can be directly controlled by examining the lung in the operative field (Fig. 6). Of course, in this instance, the contralateral lung is not protected from bronchial flooding until the bronchial tube is in place.

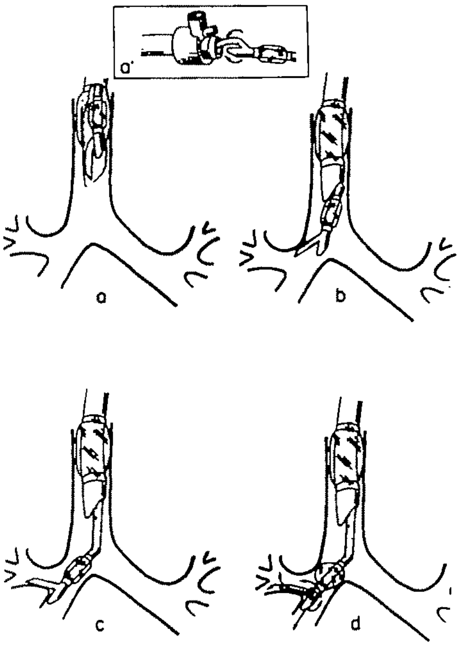


Fig. 4. Suggested method of intubation of the right main bronchus. After having deeply positioned the tracheal tube and ventilated the patient's lungs, the bronchial tube, well lubricated, is inserted (a') and pushed down into the main tube. Attention should be paid to maintaining the proper orientation of the bronchial tube during insertion. A sudden drop in the resistance to advancement of the bronchial tube and a special external ink mark, indicate that the distal extremity of the tube and its cuff have come out of the tracheal tube. Keeping the bronchial tube firmly directed it is pushed for a further few cm, until advancement is stopped by engagement of the lateral branch in the upper lobe bronchus. This denotes the correct position of the tube, avoiding obstruction of the origin of the right upper lobe bronchus. The cuff is then inflated (d) and the tubes are externally connected by means of the movable ring, which slides along the bronchial tube, keeping it firmly in position.

Results

The results of air flow and resistance determinations showed similar values in both channels (Fig. 7). In the 21 patients in which this technique has been used, arterial blood gas analysis has been carried out before, during and after one lung anaesthesia. $F\mathrm{IO}_2$ and gas flow were adjusted,[6,16-18] in order to maintain adequate arterialisation of venous blood ($P\mathrm{aO}_2 > 10.7$ kPa; $P\mathrm{aCO}_2 < 4.0$ kPa). This was achieved in all cases during one lung ventilation with a tidal volume of 7 ml/kg body weight. (SD 0.7) respiratory rate 20

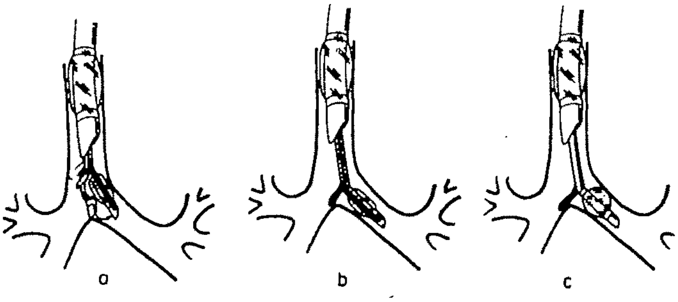


Fig. 5. Suggested method of intubation of the left main bronchus. Working as shown in Fig. 4, the appropriate bronchial tube is inserted until its tip has emerged from the tracheal tube. A guide is then inserted (a) and the properly directed tube is pushed down for a few centimetres (b). The guide is then withdrawn, the cuff inflated (c) and the tubes are externally connected as shown in Fig. 4.

breaths/minute at an FIO_2 of 0.4 (SD 0.05). Whenever possible (17 cases), the surgeon was requested to clamp the main pulmonary artery before excluding the lung from ventilation, in order to eliminate the resulting right to left shunt. In seven patients undergoing right pneumonectomy, the left main bronchus was intubated, whereas in 14 patients undergoing left pneumonectomy, the bronchial tube was introduced into the right main bronchus.

In the first three cases of right pneumonectomy, the first trial of left bronchus intubation was made without the use of a guide, by simply directing the tip bending of the bronchial tube towards the left main bronchus. In all these cases, this resulted in the right main bronchus being intubated. This is probably due to the low rigidity at body temperature of the material employed in the manufacture of the tube (PVC–silicone mixture), which reduced the hardness of the tip and

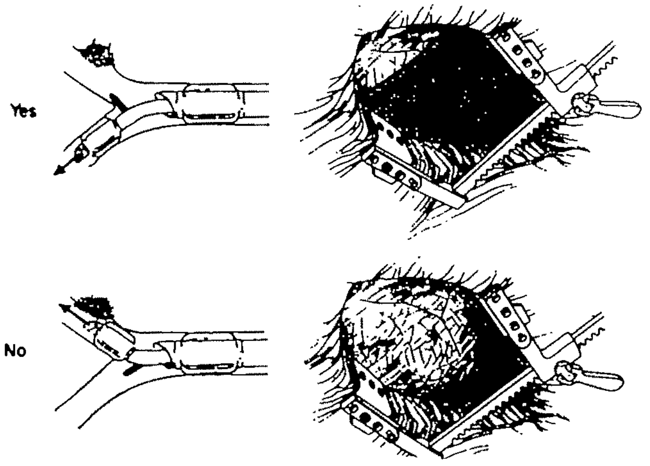


Fig. 6. Intra-operative bronchial tube position check. Is the bronchial tube in the selected bronchus (contralateral)? Yes: exposed lung deflated and motionless during the ventilation through the bronchial tube only. The correct ventilation of the contralateral lung is demonstrated by normal exhaled gas flow measured by the ventilator's spirometer. No: exposed lung expansion during ventilation through the bronchial tube only.

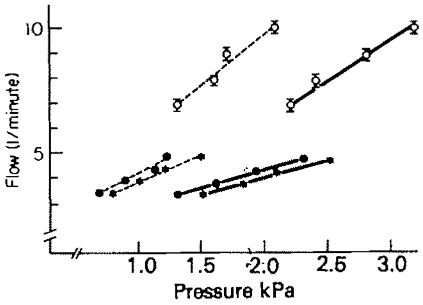


Fig. 7. Resistance of the isolated system at different air flows. (——), 10 mm ID; (——) 9.0 mm ID; (●), bronchial tube; (*), tracheal tube; (○), the whole system. Each point is the mean of three determinations (SD); the resistances shown in the graph are the maximal values recorded in a single breath (20 breaths/minute). The measurements were performed in the isolated system, so that the subjects' airway resistances were not considered.

led to bending. The bronchial tube was then removed and correctly positioned with the use of a guide, as described under Methods (Fig. 5).

No problems arose with right main bronchus intubation; the average duration of apnoea during insertion was less than 20 seconds. Visual inspection of the operative field allowed fine adjustment of the position of the bronchial tube and of inflation of its cuff, so that perfect separation of the two lungs could be obtained. The correct position of the bronchial tube was always checked by direct inspection through the cut contralateral bronchus, before performing mechanical stapling of the divided bronchus.

Discussion

One lung anaesthesia was carried out for the first time by Gale and Waters in 1932,[19] who devised and used a curved single-lumen cuffed tube that was blindly passed into the left or right main bronchus. From that period, many other methods of one lung anaesthesia were proposed, in an attempt to make the intubation technique easier and safer, and to meet anaesthetic and surgical needs fully.

From the technical point of view, the methods proposed for separating the two lungs during surgery may be summarised as follows:[5] bronchial tubes, bronchial blockers and double-lumen tubes (Fig. 8).

Bronchial tubes.[19-24] This was the first method employed for one lung anaesthesia. After the model devised by Gale and Waters,[19] a number of bronchial tubes were designed for left or right main bronchus intubation (Machray,[24] MacIntosh-Leatherdale,[20] Gordon-Green,[21] Brompton,[6] Rovenstine,[12] Magill,[25] Pallister[22]).

Some of these (Magill, Machray) were inserted under bronchoscopic control; the others were passed blindly into the selected main bronchus. These tubes must be positioned in the main bronchus of the healthy lung, and as a consequence, the 'surgical' lung is permanently excluded from ventilation while the bronchial tube is in place. An advance was achieved by fitting the tube with a tracheal cuff; in this way deflation of the bronchial cuff converts ventilation from one to two lungs without the need to withdraw the bronchial tube into the trachea.[12] These tubes allow safe one lung anaesthesia, sealing off the healthy lung. However, major disadvantages lie in the fact that blood or secretions entering the trachea from the 'surgical' lung cannot be removed; moreover, the 'surgical' lung cannot be inflated or deflated depending on surgical needs, but is permanently collapsed until one lung anaesthesia is stopped.

A further problem arises when the right main bronchus has to be intubated; in fact, due to the shortness of this bronchus, the cuff obstruction of the upper lobar bronchus is quite frequent.[4,6,12] A specially devised tube (Gordon-Green) could prevent this complication, however, although upper lobe obstruction is less probable with this tube, absolute precision is still needed to obtain a complete separation of the two lungs. In fact, if the cuff is not exactly positioned and properly inflated to ensure contact between the cuff and the surface of the bronchial wall all around the upper lobar bronchus origin, the two lungs are incompletely separated.

Bronchial blockers.[4-7,12,25-29] These devices were introduced into clinical practice by Magill in 1936. They consist of a thin lumen, cuffed tube passed, under bronchoscopic control, into the main bronchus of the lung to be operated upon. The bronchial blocker then lies lateral to a standard tracheal tube that provides ventilation of the healthy lung (Fig. 8). Thompson[27] covered the blocker's cuff with gauze, to obtain more stable contact with the mucosa and to prevent overinflation of the cuff. Crafoord[26] replaced the cuffed tube with a gauze tampon, positioned under bronchoscopic control, into the

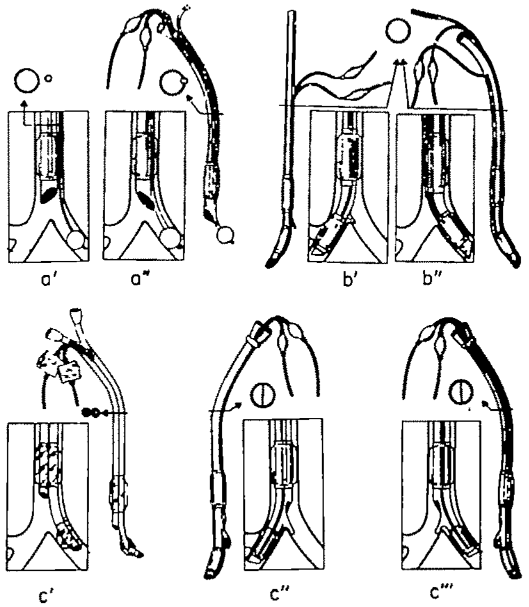


Fig. 8. The most usual methods of one-lung anaesthesia. Magill (a') and Macintosh-Leatherdale (a'') bronchial blockers. Gordon-Green (b') and Macintosh-Leatherdale (b'') bronchial tubes. Double-lumen tubes (c'), White (c'') and Carlens (c'' ') double-lumen tubes. Arrows indicate the section's shape of the air channels of each method. (From Péries F.,[4] modified).

bronchus which was to be excluded. Macintosh and Leatherdale[20] incorporated the bronchial blocker in the tracheal tube, so that the bronchial blocker could be put into place blindly during tracheal intubation.

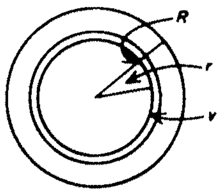
Bronchial blockers actually exclude the operated lung from ventilation and also make collapse of the lung and suction of secretions difficult. Another major disadvantage lies in the fact that they cannot be used when pneumonectomy or surgery of the carina has to be performed.

Double-lumen tubes.[1-12] These tubes are the most commonly used in thoracic surgery (Fig. 8). The first model was developed by Carlens in 1949,[3] for bronchospirometry. They consist of two air channels linked together, whose ends are blindly positioned respectively into a main bronchus and the trachea. Many types of these tubes have been proposed, either for the left (Carlens,[3] Robertshaw[8]) and right main bronchus intubation (White,[11] Robertshaw,[8] Bryce-Smith;[9-10]); each one has its own characteristics that offer particular advantages. The major advantage of these tubes lies in the fact that they allow separate ventilation of either lung. However, some problems are still found with their use. Indeed, introduction is troublesome, mainly because of their diameter which is larger than the standard tracheal tubes, and because of the shape of their tips, which hamper passage through the larynx and advancement down the trachea. Moreover, malpositioning of the tip of the tube is a frequent event; in left bronchus intubation, the most usual malposition is too deep insertion of the tube, so that the right lung is excluded from ventilation.[14,15] Major problems arise in right main bronchus intubation; in fact,. due to the shortness of the right main bronchus, absolute precision is needed to prevent the exclusion of the right upper lobe from ventilation. Moreover, separation of the two lungs is frequently incomplete with the specially designed right-sided double-lumen tubes. Another disadvantage lies in the fact that when the patient is moved after intubation, and is placed in the lateral position, the tube is easily displaced.[7]

Our method seems to solve many of these problems and to offer other advantages. A feature common to all the commercially available double-lumen tubes is that the two channels are permanently linked to each other, so that tracheal and bronchial intubation has to be carried out at the same time. The technique is, accordingly, more complex than the standard orotracheal intubation, while with our method tracheobronchial intubation is performed separately in two steps. In the second step, bronchial intubation can then be carried out with no hurry and in full safety; in fact, the presence of the main tracheal tube always provides a safe pathway for ventilation should any problems arise, for example, in abnormal anatomical conformations. In these cases, bronchial intubation may be repeated many times, as it is possible to ventilate the lungs through the tracheal tube between the trial intubations. Furthermore, as laryngoscopy is not necessary for the insertion of the bronchial tube bronchial intubation can be carried out at any time during surgery, whatever the patient's position. This aspect is of particular interest, as many unexpected situations arising in clinical practice could thus be solved.

This method of assembling the tubes allows the total external diameter of the device to be reduced compared with the double-lumen tubes commercially available, which have channels of equivalent sections. The device incorporates two air channels which have one wall in common (Fig. 2), resulting in a major section available for gas flow. The section of a standard tracheal tube of 9 mm ID (63.6 sq mm) into which a bronchial tube of 5 mm ID and 6.8 mm OD is inserted, is reduced only by the surface area of its wall (16.6 sq. mm). The final section (47 sq. mm) is equivalent to that of a 7.5 mm ID standard tracheal tube (44.1 sq mm), which is sufficient to ventilate both lungs. The combinations of tubes described above are those we considered to be the most suitable for routine clinical use in adults, when two channels with similar resistance are needed. However, any other reciprocal dimensioning of the two tubes that provides two channels with equivalent sections can be obtained by the following relationship:

$$r = \frac{\sqrt{2R^2 - v^2} - v}{2}$$



where R is the inner radius of the main tracheal tube, r is the inner radius of the bronchial tube and v is the thickness of the wall of the bronchial tube.

Although, at present, experience has been gained only in lung surgery, in our opinion advantages may be suggested in other clinical situations. The method could be favourably used in intensive care patients, when differential ventilatory schedules (differential PEEP, no or low flow in one lung) are advisable for the treatment of unilateral lung diseases (lung atelectasis,[30] massive pneumonia,[31] lung contusion or haematoma,[32–34]. In these cases, the bronchial tube may be easily positioned and removed many times a day, leaving the main tracheal tube in place. Moreover, by choosing the correct sizes of the tubes, bronchial intubation may be carried out through the nostril, a method of intubation more suitable for long term ventilatory support in intensive care patients, and so far precluded due to the size and shape of the commercially available double-lumen tubes.

Conclusions

The major advantages of this method of tracheobronchial intubation may be summarised in the following points: standard technique is used for tracheal intubation; bronchial intubation is easy and safe and can be carried out at any time during surgery, whatever the patient's position; should any problem in bronchial intubation arise, the main tracheal tube always provides a safe pathway for ventilation. This allows bronchial intubation to be attempted many times without haste, since it is possible to ventilate the patient safely.

Addendum

We have now used this method of bronchial intubation in 73 patients and are satisfied that it is superior to the use of conventional double-lumen tubes. On six occasions, the right main bronchus could not be intubated at the first attempt, but after removing the bronchial tube and ventilating via the tracheal tube, successful right bronchial intubation was achieved in each case. There has been no instance where the tube has not engaged in the right upper lobe bronchus.

Acknowledgments

The authors express their thanks to Portex Ltd. and its managers for their cooperation and prototype production. Secretarial assistance from Mrs F. Casale was most helpful and much appreciated. The authors also thank Informedical Consultants, Milan, for translation of the Italian manuscript.

References

1. Bjork VO, Carlens E, Friberg O. Endobronchial anesthesia. *Anesthesiology* 1953; **14:** 60–72.
2. Clarke AD. The white double lumen tube. A report on its use in fifty cases. *British Journal of Anaesthesia* 1962; **34:** 822–4.
3. Carlens E. New flexible double-lumen catheter for bronchospirometry. *Journal of Thoracic Surgery* 1949; **18:** 742–6.
4. Peries D. Anésthesie et réanimation en chirurgie pulmonaire d' exérèse. *Encyclopedie Medico-Chirurgicale, Editions techniques, Paris* 1974, fasc. 3, 17.09; 42240.
5. Pappin JC. The current practice of endobronchial intubation. *Anaesthesia* 1979; **34:** 57–64.
6. Churchill-Davidson HC. Thoracic anaesthesia. In Churchill-Davidson, ed. *A practice of anaesthesia*, 4th edn. London: Lloyd-Luke Ltd, 1978: 465–80.
7. Le Houeller J. Anestesia nella chirurgia polmonare. In Nadia du Bouchet, Jaqueline Passelecq *eds. Anesesia.* Marrapese, Roma, 1982, Vol. 2, pp. 1383–7.
8. Robertshaw FL. Low resistance double-lumen endobronchial tubes. *British Journal of Anaesthesia* 1962; **34:** 576–9.
9. Bryce-Smith R. A double-lumen endobronchial tube. *British Journal of Anaesthesia* 1959; **31:** 274–5.
10. Bryce-Smith R, Salt R. A right-sited double lumen tube. *British Journal of Anaesthesia* 1960; **32:** 230–1.
11. White GMJ. A new double lumen tube. *British Journal of Anaesthesia* 1960; **32:** 232–4.
12. Collins VC. Endobronchial technique. In *Principles of anaesthesiology* Lea and Febiger, eds. Philadelphia: Collins, 1976: 390–6.
13. Hayes B. Respiratory obstruction due to faulty Carlens endotracheal tube. *Lancet* 1961; **21:** 1205–6.
14. Wilkinson PL, Ham J, Miller RD. Double lumen endotracheal tube for pneumonectomy. In Wilkinson, Ham, Miller, eds. *Clinical anaesthesia. Case selections from the University of California, San Francisco.* St Louis: C.V. Mosby Co., 1980: 97–100.
15. Stark DL. *Practical points in anesthesiology.* Flyshing, New York: Medical Examination Publishing Co., 1974.
16. Torda TA, McCulloch CH, O'Brien HD, Wright JS, Horton DA. Pulmonary venous admixture during one-lung anaesthesia. *Anaesthesia* 1974; **29:** 272–9.
17. Khanam T, Branthwaite MA. Arterial oxygenation during one-lung anaesthesia (1). A study in man. *Anaesthesia* 1973; **28:** 132–8.
18. Khanam T, Branthwaite MA. Arterial oxygenation during one-lung anaesthesia (2). *Anaesthesia* 1973; **28:** 280–90.
19. Gale JW, Waters RM. Closed endobronchial anesthesia in thoracic surgery: preliminary report. *Journal of Thoracic Surgery* 1932; **1:** 432–7.
20. MacIntosh R, Leatherdale RAL. Bronchus tube and bronchus blocker. *British Journal of Anaesthesia* 1955; **27:** 556–7.
21. Green R, Gordon W. Right lung anaesthesia. Anaesthesia for left lung surgery using a new right endobronchial tube. *Anaesthesia* 1957; **12:** 86–93.
22. Pallister WK. A new endobronchial tube for left lung anaesthesia, with specific reference to neurostructive pulmonary surgery. *Thorax* 1959; **14:** 55–7.
23. Vellacott WN. A new endobronchial tube for bronchopleural fistula repair. *British Journal of Anaesthesia* 1954; **26:** 442–4.
24. Machray R. Anaesthesia for the surgical treatment of chest disease. *Tuberculosis Index* 1958; **13:** 172–8.
25. Magill IW. Anaesthesia in thoracic surgery, with special reference to lobectomy. *Proceedings of the Royal Society of Medicine* 1936; **29:** 643–53.
26. Crafoord C. On technique of pneumonectomy in man; critical survey of experimental and clinical development and report of author's material and technique. *Acta Chirurgica Scandinavica* 1938; **81** (Suppl. 54): 1–142.
27. Rusby NL, Thompson VC. Carcinoma of the lung: diagnosis and surgical treatment. *Postgraduate Medical Journal* 1943; **19:** 44–53.
28. Sturzbecher F. Die Blockade feuchter Lungen mit einem spezial Katheter. *Anaesthesist* 1953; **2:** 151–2.
29. Green R. Endobronchial tube and blocker for right upper lobe. *Anaesthesia* 1958; **13:** 349–52.
30. Murray JF. Treatment of acute total atelectasis. Use of a double lumen tube. *Anaesthesia* 1985; **40:** 158–62.
31. Powner DJ, Eross B, Grenvik A. Differentiated lung ventilation with PEEP in the treatment of unilateral pneumonia. *Critical Care Medicine* 1977; **5:** 170–2.
32. Kuetan V, Graziano G, Carlon C, Howland W. Acute pulmonary failure in asymmetric lung disease. Approach to management. *Critical Care Medicine* 1982; **10:** 114–8.
33. Carlon C, Ray C Jr, Klein R, Goldiner PL, Miodownik S. Criteria for selective positive end-expiratory pressure and independent synchronized ventilation of each lung. *Chest* 1978; **74:** 501–7.
34. Gallager TJ, Banner MJ, Smith RA. A simplified method of independent lung ventilation. *Critical Care Medicine* 1980; **8:** 396–9.

Anaesthesia, 1986, Volume 41, pages 527–532

APPARATUS

A comparison of five heat and moisture exchangers

MAIRE SHELLY, D. W. BETHUNE AND R. D. LATIMER

Summary

Five heat and moisture exchangers were investigated to compare their efficiency of humidification, their ability to filter bacterial spores and their various physical properties. The results are presented and the various mechanisms of heat and moisture exchange are reviewed. The Pall Ultipor BB50, because of its hydrophobic properties, has a slightly different action from heat and moisture exchangers already in use. The place of the Pall Ultipor BB50 in clinical practice is discussed.

Key words

Equipment; heat and moisture exchanger.
Humidifier; humidification.

Many types of heat and moisture exchanger (HME) are currently available for use with patients requiring long or short term ventilation. HMEs provide adequate humidification of the patient's respiratory tract,[1-3] reduce heat loss peroperatively,[4,5] and are cheaper and more convenient to use than hot water humidifiers. HMEs also reduce contamination of ventilator tubing and valves by water. This minimises damage to equipment, prolongs its life and helps to reduce the likelihood of ventilator malfunction and its consequent risk to the patient.[6]

Recently, the Pall Ultipor BB50, already in widespread use as a breathing system filter, has been shown to be an efficient HME[4] with the additional advantage of being an effective bacterial filter.[7]

Theoretical considerations

Early condenser humidifiers such as the Garthur, had layers of wire mesh. These have been superceded by several hygroscopic HMEs. The hygroscopic effect is achieved in a different way by each device; the Portex Humid-Vent has a paper element coated with calcium chloride, the Siemens-Elema Servo humidifier has a fibreglass element and the Engström Edith contains a polypropylene fibre cylinder coated with lithium chloride. The latter two HMEs are said to have antibacterial properties in addition; the Siemens appears to trap bacteria,[8] but the bacteriostatic action claimed for both this and the Edith have recently been questioned.[9,10]

The most recent addition to the HME group is the Pall Ultipor BB50 Breathing System Filter

---

Maire Shelly, FFARCS*, Research Assistant, Department of Anaesthetics, Addenbrooke's Hospital, Cambridge, CB2 2QQ, D.W. Bethune, FFARCS, Consultant Anaesthetist, R.D. Latimer, FFARCS, Consultant Anaesthetist, Papworth Hospital, Papworth Everard, Huntingdon.

*Dr M.P. Shelly is in receipt of a grant from Napp Laboratories Ltd.

0003–2409/86/050527 + 06 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

with its folded ceramic fibre element; this has a large hydrophobic surface area and provides not only efficient bacterial filtration, but also effective humidification of inspired gases.[4]

The theoretical mechanism of action cf condenser humidifiers, described by Mapleson,[11] was developed by studying the Garthur humidifier and is thought not to apply to more recent HMEs. Hygroscopic HMEs are more efficient than suggested by the Mapleson theory because a proportion of the water vapour passing through the device during expiration is adsorbed onto the hygroscopic part of the element and is then collected by dry gases on inspiration.

No liquid water is formed and the temperature change involved is insignificant, so this type of HME is not a condenser humidifier in the true sense. The Edith has only a hygroscopic element, whereas a hygroscopic portion is used in conjunction with a classical condenser humidifier in the Siemens to improve its efficiency.[12]

Other HMEs, without hygroscopic properties, have also been found to be more efficient than expected. The discrepancy has been attributed to deductions made in developing the original theory.[13,14] The first deduction made (the lowest temperature associated with the humidifier will be that of the fresh gas,[11]) may not be the case under all circumstances. The statement does not take into account any reduction in temperature that occurs as water droplets are vaporized from the humidifier element. A temperature gradient may be set up within the humidifier as the latent heat of vaporization is taken from the fresh gas; this has been demonstrated experimentally[14] and can be derived from other experimental data.[4] The distal part of the HME can, therefore, be cooler than its surroundings. Gas leaving the HME will be saturated at the lowest temperature achieved, but this is not necessarily the fresh gas temperature. The temperature levels within the HME will vary with the phase of respiration, the tidal volume, the relative humidity of the inspired gas and the heat capacity, conductivity and water content of the HME element.[14] The water lost from the HME will, therefore, depend on all these factors.

The Garthur humidifier, on which the original theory was based, does not develop temperature gradients within the HME because it has metal gauzes with high conductivity; it thus complies with Mapleson's deductions.

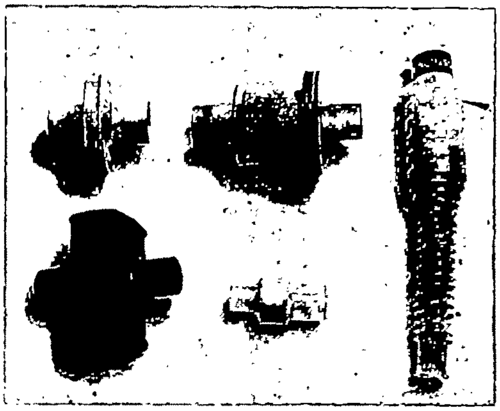


Fig. 1. Heat and moisture exchangers, clockwise from top left: Garthur humidifier, Siemens-Elema Servo humidifier, Engström Edith, Portex Humid-Vent and Pall BB50 breathing system filter.

Method

Five commonly available HMEs were studied: the Garthur, the Portex Humid-Vent, the Siemens-Elema Servo humidifier, the Engström Edith and the Pall Ultipor BB50 (Fig. 1). Several factors were investigated, based on features considered desirable in an ideal HME (Table 1).

The ability of the HMEs to conserve water was assessed using the method described by Walker and Bethune.[15] The various HMEs were placed between apparatus representing a patient; a ventilator and thermostatically controlled hot water bath and a collection and measurement system; a heat exchanger to condense most of the water vapour into a measuring cylinder, a hygrometer to measure the humidity and a respirometer to measure the volume of the cooled gas. The amount of water lost through the HME was measured for each humidifier. This method produces results approximating to those theoretically expected and a reproducible pattern of results is obtained with different end expiratory

Table 1. The properties of an ideal heat and moisture exchanger

Efficient retention of heat and moisture
Effective bacterial filter
Safe
Minimum number of airtight connexions
Low resistance to airflow
Low dead space
Light weight
Convenient for storage
Disposable or easily sterilised
Cheap

temperatures. Twelve separate experiments were performed on each design of HME, six using room air and six with dry anaesthetic gases. Each experiment used a new HME and measurements were made at intervals during each run. The end expiratory temperature was maintained at 34.5°C throughout, corresponding to tracheal temperature.[15]

The efficacy of the HME as a bacterial filter was assessed using a modification of an established technique.[16] An aerosol containing spores of *Bacillis subtilis* var. *gobigii* was passed through the HMEs and the residue collected on blood agar plates using a slit sampler (Castella). The plates were then incubated for 24 hours before counting the colonies. Three humidifiers of each type were tested and the total number of spores in the aerosol was estimated using an all-glass impinger. Spores were used since they are more hardy than bacteria and these particular spores are approximately the same diameter as coliforms such as *Pseudomonas*, an important contaminant. Attempts were also made to reproduce the data in the information sheet provided with the Edith, showing the survival time of some common bacteria and fungi within the Edith element.

The minimum number of airtight connexions was taken to be the number of standard fittings between the top of the tracheal tube and the breathing system, together with any connexions within the HME. This was used to indicate the liability of the HME to leakage or disconnexion. Resistance across the HMEs was measured at a 30 litres/minute flow using a pneumotachograph. A catheter mount was added to the HME, if appropriate and the results expressed in Pascals.

Internal volume was measured by filling both sides of the HME with water and repeating with a catheter mount as necessary; the volume of water used was measured before filling the devices. The weight of the humidifiers was measured using an electronic balance (IE DSK2). The cost per unit of the various humidifiers was calculated from the manufacturers' quoted price for hospital supply in the largest available quantity. The cost of a disposable catheter mount was added where required and prices were also obtained for the re-usable outer cases.

Results

The hourly water loss from the HMEs is shown in Fig. 2 for both room air and dry anaesthetic gases. Measurements were also taken using both

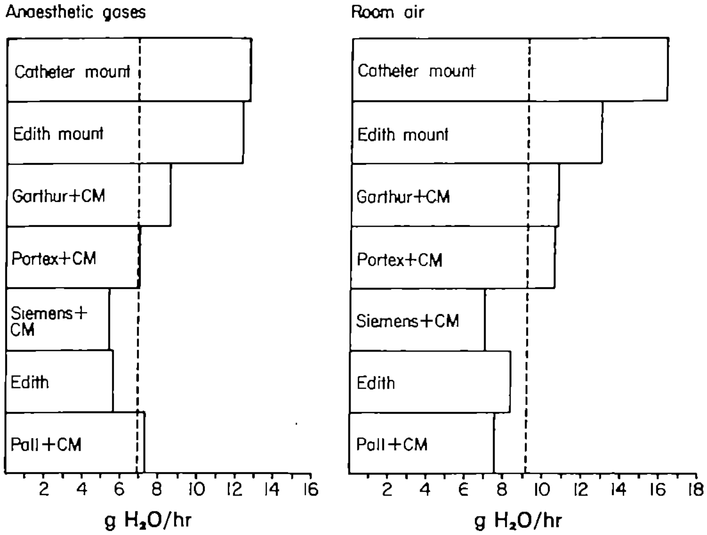


Fig. 2. Hourly water loss through heat and moisture exchangers with catheter mount (+CM) where appropriate. Fresh gas flow 7 litres/minute with room air: temperature 23.5°C, relative humidity 40 percent; with anaesthetic gases: temperature 19.3°C, relative humidity <10 percent. Dotted line represents theoretical minimum loss according to Mapleson's theory.

Table 2. Physical properties of heat and moisture exchangers

HME	Number of connexions	Resistance (Pa)		Internal volume (ml)		Weight (g)	
		−CM	+CM	−CM	+CM	−CM	+CM
Garthur	6	18.0	69.0	29.0	57.0	53.9	103.6
Portex	5	87.0	138.0	12.5	40.5	10.6	60.3
Siemens	6	32.0	83.0	88.5	116.5	41.8	91.5
Edith	3	—	75.0	—	92.0	—	18.8
Pall	5	50.0	100.0	75.0	103.0	46.9	96.6

−CM, without catheter mount, Edith omitted as humidifier incorporated into catheter mount.
+CM, with catheter mount, Edith included alone.

a straight and a corrugated catheter mount (the corrugated catheter mount used was the Edith HME with its elements removed). Using room air, the catheter mounts reduced the water loss from the theoretical value.[15] The Garthur and Portex HMEs reduced the loss still further and the Pall, Edith and Siemens humidifiers, by virtue of their hygroscopic and hydrophobic properties, caused the water loss to fall below the level which is theoretically obligatory. The pattern of results using dry anaesthetic gases was slightly different. The water loss through the Pall BB50 and the corrugated catheter mount was unchanged, while with the other HMEs, water loss decreased when dry gases were used.

On bacteriological investigation, only the Pall BB50 filter was effective, removing 99 percent of spores passed through it. The other HMEs had no measurable effect. No confirmation could be made of the bacterial survival times in the Edith; the growth of all bacteria tested was unaffected in spite of the 0.1 percent chlorhexidine with which the Edith element is impregnated. Comparison of the HMEs regarding number of connexions, resistance, internal volume and weight is shown in Table 2 and cost is shown in Table 3.

Discussion

Humidification

The water loss studies indicate that three devices, the Siemens-Elema Servo humidifier, the Engström Edith and the Pall Ultipor BB50, were able to mimic the function of the upper respiratory tract.[3] Humidification of both dry gases and room air was achieved to the levels found in nose breathing normal subjects.[17] The other two devices, the Portex Humid-Vent and the Garthur humidifier, provided adequate humidification when dry gases were used, but failed to reach physiological levels of humidity with room air. The Garthur and Portex HMEs produced water losses above the theoretical minimum, while the Siemens, Edith and Pall were capable of performing more efficiently than suggested by Mapleson's theory, as described above.

Table 3. Comparative cost of heat and moisture exchangers

HME	HME/HME insert (£)		Outer case (£)
	−CM	+CM	
Garthur	2.25	2.90	31*
Portex	0.80	1.45	—
Siemens	0.63	1.28	18*
Edith	—	1.08	—
Pall	2.92	3.53	—

*Re-usable component, requires cost of sterilisation to be taken into account.
−CM, without catheter mount, Edith omitted, humidifier incorporated into catheter mount.
+CM with catheter mount, Edith included alone.

Bacterial filtration

The Pall Ultipor BB50 proved to be an effective bacterial filter, removing 99 percent of the bacterial spores in the aerosol. The other devices appeared to have no significant antibacterial effect.

Physical properties

There were six points of connexion between the top of the tracheal tube and the breathing system with the Garthur and Siemens HMEs as both have an outer case and replaceable insert. This provides an increased likelihood of disconnexion or gas leakage, particularly as increasing use of the outer case may damage its screw thread. This problem is neatly solved in the Edith, where the HME element is incorporated into a corrugated catheter mount, thus removing the need for additional connexions. The connexions on all the devices were standard 22-mm and 15-mm male and female.

The resistance was low for the Garthur and Siemens HMEs and higher for the Portex and Pall. When the resistance of the catheter mount was included, however, the results became more comparable and only the Portex HME had a resistance to more than 100 Pa at a 30 litre/minute flow. The Portex had the lowest internal volume, followed by the Garthur; the more bulky Siemens and Pall HMEs had the highest volumes but the Edith compared favourably when the volume of a catheter mount was added. The same principle applied to the HME weights. The Portex was the lightest and the Garthur the heaviest, the Siemens and Pall were also comparatively heavy, but when the weight of the catheter mount was added to these, the Edith was by far the lightest.

An important consideration is cost and this may be difficult to assess accurately. For example, the Siemens humidifier is relatively cheap when the insert is considered alone, but add to this the cost of a catheter mount, the case and its sterilisation and the total becomes appreciable. The price of a disposable catheter mount and the re-usable outer case is shown in Table 3, but the cost of sterilisation is more difficult to establish, since it will vary with the method used. These considerations mean that the Edith is the cheapest and the Garthur the most expensive HME. The Pall, by virtue of its antibacterial properties, may recoup some of its relatively high cost by reducing the frequency of ventilator tubing replacement or sterilisation.

Conclusion

The Engström Edith, Siemens Servo humidifier and Pall Ultipor BB50 provide adequate humidification of the respiratory tract with both room air and dry anaesthetic gases. The Pall BB50, however, has the added advantage of being an efficient bacterial filter, which may be important in the infected or immunocompromised patient, or in the intensive care unit.

Addendum

This study was undertaken using the Pall Ultipor BB50 breathing filter. Since its completion, two further filters have been marketed, the BB50T and the BB22/15. These are functionally identical to the BB50 and provide a range of connector sizes.

Acknowledgments

We wish to thank Julie Matthews of Papworth Hospital for her invaluable assistance with the bacteriological investigations.

References

1. Weeks DB. Humidification during anesthesia. *New York Journal of Medicine* 1975; **75:** 1216–8.
2. Tattersal M. Should we humidify our anaesthetic gases? A review. *Anaesthesia Points West* 1984; **15:** 17–19.
3. Bethune DW, Shelly MP. Hydrophobic versus hygroscopic heat moisture exchangers. *Anaesthesia* 1985; **40:** 210–1.
4. Chalon J, Markham JP, Ali MM, Ramanathan S, Turndorf H. The Pall Ultipor breathing circuit filter—an efficient heat and moisture exchanger. *Anesthesia and Analgesia* 1984; **63:** 366–70.
5. Linko K, Honkavarra P, Nieminen M-T. Heated humidification in major abdominal surgery. *European Journal of Anaesthesiology* 1984; **1:** 285–91.
6. Hilton PJ, Clement JA. Surgical emphysema resulting from a ventilator malfunction. *Anaesthesia* 1983; **38:** 342–5.
7. Latham MJ. Bacterial removal efficiency of Pall Ultipor Anaesthesia/Breathing Filter BB50. *Technical Report* BM2044, Pall Europe Ltd.
8. Stange K, Bygdeman S. Do moisture exchangers prevent patient contamination of ventilators? *Acta Anaesthesiologica Scandinavica* 1980; **24:** 487–90.
9. Leigh JM, White MG. A new condenser humidifier. *Anaesthesia* 1984; **39:** 492–3.

10. Bygdeman D, von Euler C, Nystrom B. Moisture exchangers do not prevent patient contamination of ventilators. A microbiological study. *Acta Anaesthesiologica Scandinavica* 1984; **28:** 591–4.
11. Mapleson WW, Morgan JG, Hillard EK. Assessment of condenser humidifiers with special reference to a multiple-gauze model. *British Medical Journal* 1963; 300–5.
12. Gedeon A, Mebius C. The hygroscopic condenser humidifier. *Anaesthesia* 1979; **34:** 1043–7.
13. Revanas B, Lindholm CE. The foam nose—a new disposable heat and moisture exchanger. *Acta Anaesthesiologica Scandinavica* 1979; **23:** 34–9.
14. Revenas B, Lindholm CE. Temperature variations in disposable heat and moisture exchangers. *Acta Anaesthesiologica Scandinavica* 1980; **24:** 237–40.
15. Walker AKY, Bethune DW. A comparative study of condenser humidifiers. *Anaesthesia* 1976; **31:** 1086–93.
16. Newsome SWB. A test system for biological safety cabinets. *Journal of Clinical Pathology* 1979; **27:** 585–9.
17. Dery R. The evolution of heat and moisture in the respiratory tract during anaesthesia with a non-rebreathing system. *Canadian Anaesthetists' Society Journal* 1973; **20:** 296–307.

Anaesthesia, 1986, Volume 41, pages 533–537

Forum

Anaesthetic management and postoperative care of cardiac surgical patients in a general recovery ward

C. Aps, MB, BS, FFARCS, Consultant Anaesthetist, J.A. Hutter, FRCS, Senior Surgical Registrar, B.T. Williams, FRCS, Consultant Cardiothoracic Surgeon, Departments of Anaesthetics and Cardiothoracic Surgery, St Thomas' Hospital, London SE1 7EH.

Summary

The postoperative care of 143 cardiac surgical patients has been successfully conducted in a general surgical recovery ward. Admission was limited to overnight stay only and all but two patients were returned to the general ward the following day. There were no deaths. The intra-operative anaesthetic management was considered to have played an important part in the success of this technique.

Key words

Anaesthesia; cardiovascular.
Surgery; cardiopulmonary bypass.

The demands for open heart surgery, especially aortocoronary bypass grafting, tend to exceed the postoperative facilities available. In an attempt to overcome the problems of last-minute operation cancellations due to blocked intensive care beds, a proportion of routine cardiac surgical cases were managed in a general surgical recovery ward. Early extubation is by no means a new concept in these patients, but the implications to the patient in relation to the postoperative management in a general surgical recovery area posed unique problems. This paper describes the particular anaesthetic approach involved.

Method

The general surgical recovery ward. This purpose-built area (separate from the intensive care ward) was designed to cope with the immediate postoperative care of a variety of surgical patients for up to 12 theatres. It has facilities for 18 patients, some of whom may be kept overnight for special observation. Limited equipment is also available for intermittent positive pressure ventilation (IPPV), for direct arterial and venous pressure monitoring, and continuous electrocardiography. Maximum duration of admission is limited to overnight stay only. The majority of the nursing staff are not trained in intensive care, although the senior members have cardiac or intensive care experience.

Table 1. Patients managed in the general recovery ward (1983–1985)

Operations performed	Total	First group[1]
Coronary artery revascularisation	130	98
Repair atrial septal defect	5	4
Mitral valve replacement	3	0
Aortic valve replacement	2	0
Pulmonary valvotomy	1	1
Cardiomyotomy (hypertrophic obstructive cardiomyopathy)	1	0
Fontan's procedure	1	0
	143	103

Patients and aims. Over two years (1983–85) 143 patients were managed in this general recovery ward following cardiac surgery. The types of operation performed are shown in Table 1. Detailed data collected from the first 103 patients managed in this way, which provided the basis for a report published in a surgical journal,[1] are shown in Table 2. Patients were initially selected pre-operatively for 'recovery' rather than 'intensive care' on criteria that basically excluded gross functional limitations or poor ventricular function. Later we found that selection tended to be made on the relative fitness of the patient to be admitted to the

---

Correspondence to: C. Aps, MB, BS, FFARCS, Department of Anaesthetics, St Thomas' Hospital, London SE1 1EH.

0003–2409/86/050533 + 14 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Table 2. Operative records from the first 103 patients[1] (mean values, SD, range)

Age	49(10.7) (21–67)
Weight	74.1(9.7) (54–87)
Cardiopulmonary bypass	
Duration (minutes)	76(31)
Ischaemic time (minutes)	39(24)
Temperature (°C)	32
Ejection fraction (%)	58(11.1) (35–75)
Mean number of distal anastomoses (CABG)	3.1 (1–5)

recovery ward as compared with the others on that day's list. The criteria that proved most reliable, however, were based on their performance following cardiopulmonary bypass, and a decision was made at that time whether to elect for general recovery ward or intensive care ward management. Indeed, four out of the first 107 patients were redesignated in theatre to intensive care ward rather than recovery ward management because of intra-operative problems.

Postoperative ventilation equipment was available, but it was felt that an elective attempt should be made to extubate on the operating table. The criteria for extubation were to be no different from those already practised, namely that the patient should be awake and neurologically alert, be able to maintain adequate ventilation whilst breathing spontaneously, have a stable circulation and be warm, with a minimal core–peripheral temperature gradient. Added to these aims, the postoperative management was to be kept as simple as possible, in that intravenous infusions of potent vasodilators or inotropes were avoided and nursing care was limited to manoeuvres already adopted by the general recovery ward nurses.

Drugs used for anaesthesia. High dose opioid anaesthesia was thought to be inappropriate for immediate postoperative extubation. Likewise, the routine addition of an oral benzodiazepine to the papaveretum and hyoscine premedication was abandoned, but oral beta adrenoceptor blockade with or without calcium antagonist medication was continued up to premedication. Intravenous midazolam in small doses (2–5 mg) was administered in the anaesthetic room to cover the insertion of intravenous, radial arterial and internal jugular cannulae under local anaesthetic. Anaesthesia was induced with fentanyl 100 μg, etomidate 10–15 mg, together with pancuronium 0.1 mg/kg. Cardiovascular responses to induction and intubation were treated with the appropriate intravenous agents. Before cardiopulmonary bypass, maintenance of anaesthesia was with nitrous oxide in oxygen with the addition of either enflurane or halothane, according to the haemodynamic state. Any hypertensive responses to surgery were attenuated with intravenous nitroglycerine or alpha and beta adrenoceptor blockade.

Early in the series, sleep was maintained during bypass with small increments of fentanyl or etomidate, together with pancuronium for neuromuscular blockade. It soon became apparent that the latter, used in doses to prevent diaphragmatic movement during hypercarbic conditions, presented difficulties with reversal at the end of the procedure. Atracurium was substituted and used during bypass in intermittent doses of 5–25 mg. Likewise, alfentanil in 1 mg increments (to a total of 2–3 mg) was used instead of fentanyl at the institution of and during bypass and rewarming. After extracorporeal circulation, anaesthesia was maintained with 66 percent nitrous oxide in oxygen, with further increments of fentanyl if required. The total operative dose of fentanyl was limited to 250 μg. There were no recorded cases of intra-operative awareness.

At the end of the operation, neostigmine 2.5 mg and glycopyrronium 0.6 mg were used to reverse neuromuscular blockade. The patients' tracheas were extubated when the patients were awake, but supine, on the operating table, before they were transferred to the recovery ward bed and sat up. Again, experience with the first few patients demonstrated an incidence of early postoperative confusion, unrelated to respiratory depression. This was usually reversed by physostigmine 1–3 mg intravenously. This agent was administered routinely to all subsequent patients, and the incidence of postoperative confusion fell to zero. Restlessness or pain were adequately treated with intravenous morphine.

Intra-operative circulatory manipulation. An aggressive approach was adopted in order to restore normal arteriovenous tone, peripheral perfusion and temperature by the end of the operation. At the same time, pharmacological agents were administered in an attempt to obtund the anticipated vasoconstriction and hypertension associated with arousal and extubation.

In order to optimise whole-body heat exchange during rewarming, sodium nitroprusside or glyceryl trinitrate was infused at the maximum rate that still allowed for an adequate arterial perfusion pressure. Similarly, temperature after-drop was attenuated by careful attention to patient insulation, a warming mattress, and an efficient, lagged humidification system which provided airway temperatures in excess of 40°C (Bennett-Cascade humidifier). Cardiopulmonary bypass was not discontinued until core (nasopharyngeal) temperature was around 38°C.

During weaning from bypass, vasodilator therapy was continued in order to reduce afterload, improve myocardial efficiency and to reverse abnormal vasoconstrictor tone associated with extracorporeal circulation. Usually, this was achieved with glyceryl trinitrate together with incremental doses of phentolamine. Relatively small doses of vasodilators necessitated relatively large volume replacements at this stage in order to maintain an adequate systemic arterial pressure. The right atrial and estimated pulmonary arterial pressures were subsequently maintained within physiological limits with two units of the patient's own blood, harvested prior to bypass, and with fresh frozen plasma. The hypotensive response to protamine appeared to be minimised by the preceding vasodilatation and volume augmentation, as were further transfusion requirements following bypass. During closure, the intravenous infusion of vasodilators was discontinued, and providing that the systemic arterial pressure allowed (systolic greater than 100 mmHg, mean arterial pressure in excess of 60 mmHg), was replaced with doses of hydralazine to a total of 20 mg. Hypertension with tachycardia was controlled using small doses of labetalol. Nitroglycerine topical paste was applied to the forehead.

After extubation, and in the postoperative period, 'hypertension', defined here as a systolic arterial pressure in excess of 120 mmHg, was attenuated with further doses of labetalol or hydralazine.

Haemostasis, coagulation, urine and electrolytes. Strict surgical discipline was required to achieve surgical haemostasis before closure. Total protamine administration was based on a 2:1 heparin reversal regime, with the second aliquot administered by infusion.[2] Coagulation was enhanced by fresh frozen plasma and with the patient's autotransfused units of whole blood.

Extracorporeal haemodilution was reversed by a frusemide-induced diuresis, which was also expected to attenuate the expected increases in ventricular filling pressures associated with any increase in venocapacitance tone postoperatively. Serum potassium was maintained near 5 mmol/litre in order to reduce ventricular dysrhythmic potential.

Nurses' instructions and postoperative management. Antibiotic and topical nitrate therapy were routinely prescribed. Analgesia was provided by increments of morphine (5 mg intravenously) or papaveretum (10–15 mg intramuscularly). It was not our experience that pain relief was a particular problem in this group of patients, although we have no objective evidence to support this. Arterial blood gas and serum potassium estimations were performed regularly, and the nurses were instructed to keep the serum potassium within prescribed limits by the administration of potassium supplements. Arterial blood pressure control was normally achieved with hydralazine 10 mg, to be given intravenously as required, if the systolic blood pressure rose above 120 mmHg. Occasionally, a doctor would administer additional therapy in the form of bolus doses of labetalol. Infusions of vasodilators or inotropes were not used. In an attempt to avoid the circulatory effects of hypothermia, patient exposure was kept to a minimum, a state of affairs that appeared easier to achieve in the recovery ward than the intensive care environment. Lignocaine was administered by infusion pump to two patients who exhibited ventricular ectopics.

Peripheral (toe) and rectal or axillary temperatures were recorded. The ECG and direct arterial pressures were monitored continuously, and the central venous pressure was measured using a water manometer. Table 3 lists the pressure, temperature and blood gas measurements recorded initially, and 2 hours after admission to the general recovery ward of the first 103 patients studied.

The patients were discharged to the ward on the morning following operation. The total duration of hospital stay was 9.05 (SD 2) days.

Postoperative complications. Out of 143 patients, three required short-term IPPV (less than 1 hour) for anaesthetic reasons. One more, who had a mitral valve replacement, required overnight ventilation and subsequent transfer to the intensive care unit for further respiratory support because of severe pre-existing pulmonary disease. Three patients required further surgery for excessive bleeding, and were extubated following this. Two patients developed unheralded ventricular fibrillation; both were resuscitated successfully, but one, who had evidence of myocardial

Table 3. Recovery ward recordings from first 103 patients (mean values, SD)

Measurement	On admission	2 hours later
Core temperature (°C)	36–38	36–38
Mean peripheral (toe) temperature (°C)	33(1.97)	34.8(1.57)
Systolic blood pressure (mmHg)	120(26.8)	113.6(12.4)
CVP (from sternal angle cmH_2O)	0.8(2.3)	1.0(1.6)
Blood gas analysis data from 100 patients; spontaneous ventilation oxygen enriched air[1] (mean values, SD, range)		
pH	7.38(0.054)	7.39(0.149)
	(7.28–7.51)	(7.34–7.49)
$P\text{aO}_2$ (kPa)	15.33(7.2)	17.60(5.33)
	(6.13–25.33)	(9.60–25.33)
$P\text{aCO}_2$ (kPa)	5.51(0.79)	5.35(0.84)
	(3.47–8.27)	(3.87–6.93)

infarction, required a period of intensive care ward management.

The chest X rays taken on the first postoperative day were examined by an independent radiologist. The lung fields were clear in 47 percent, with minor atelectasis demonstrated in 32 percent, major atelectasis in 5 percent and small pleural effusions in 16 percent.

Discussion

It has been clearly shown that a proportion of post cardiopulmonary bypass patients can be safely managed in a general surgical recovery ward. This has obvious advantages to any cardiothoracic unit in terms of cost and available postoperative facilities. It also casts doubt on the necessity for true intensive care facilities for all cardiac surgical patients.

The original aims were to manage the patient after extubation, neurologically alert, peripherally warm, and with drug and fluid regimens designed to require a level of nursing experience already established in a general recovery ward environment. The surgical management has been described elsewhere.[1] The part that the anaesthetic management plays in influencing the success of this manoeuvre warrants a little discussion.

Intra-operative vasodilatation and normothermia. Active vasodilator therapy during rewarming is a well-established technique, shown to minimise temperature after-drop following cardiopulmonary bypass.[3] Active core warming with the aid of an efficient ventilator humidifier is more contentious.[4,5] but in our experience allowed for the maintenance of normal core temperature by the end of the procedure, which we were unable to achieve before its use. A warm periphery fulfils one of the normal criteria for extubation.

Aggressive arteriovenous dilatation following cardiopulmonary bypass, together with volume augmentation at that stage, allowed complete transfusion of the residual volume from the oxygenator, whilst avoiding inappropriate preload. Further volume requirements and subsequent control of blood pressure was routinely managed by the nursing staff without difficulty. Indeed, it was our impression that suitable intra-operative vasodilatation and restoration of vascular volumes, approximating to the physiological, simplified circulatory control postoperatively. Certainly, potent drugs such as sodium nitroprusside were unnecessary, whilst quite strict limitations in systolic blood pressure (no greater than 120 mmHg systolic) were achieved using bolus doses of hydralazine, and, occasionally, labetalol.

Hypertension following coronary artery surgery, which can have serious implications for the patient, has been attributed to an increase in alpha- and beta-adrenergic drive, and consequently the use of labetalol has been shown to be effective in its treatment.[6] Such adrenergic drive is enhanced by hypothermia,[7] and the avoidance of heat loss would also be expected to be beneficial in terms of achieving relative haemodynamic stability postoperatively.

Anaesthesia and arousal. Small doses of fentanyl with halogenated anaesthetic agents before bypass proved haemodynamically satisfactory. Bolus doses of alfentanil during bypass eliminated difficulties with arousal, without allowing intra-operative awareness. The use of atracurium during extracorporeal circulation is logical in that its molecular degradation is delayed under hypothermic conditions.[8] Quite small doses of atracurium appear to provide profound neuromuscular blockade following earlier paralysis with pancuronium, without compromising reversal in the fully warmed patient. This is in keeping with previous observations,[9] and with recent evidence that combinations of competitive neuromuscular blockers have a potentiating effect.[10]

Pre-induction midazolam sedation may have contributed to the ease of anaesthetic control.[11] The avoidance of atropine, and its substitution with glycopyrronium, modified inappropriate changes in pulse rate associated with reversal[12] and its lack of central effects may have contributed to the lack of postoperative confusion.[13] It is assumed that physostigmine was also advantageous in this context, bearing in mind the central anticholinergic effects associated with many anaesthetic agents and its non-specific arousal properties.[14] The use of specific opioid antagonists was unnecessary, and substituted by careful clinical observation and repeated blood gas analysis in those patients who appeared to be underventilating. Only three patients required a short period of postoperative ventilation until they were fully awake, and all of these instances occurred before use of alfentanil on bypass. Analgesia with intravenous boli of morphine was satisfactory and did not produce clinically significant hypoventilation or obtund patient cooperation.

'Early' extubation. The term 'early' is misleading, as it implies extubation before normal criteria for extubation are met. No patient was extubated without meeting these conditions, which were fulfilled in all but four patients by the end of the operation. It is interesting to note that the incidence of radiological lung changes seen on the following day is less than generally accepted in patients whose lungs are routinely ventilated following cardiac surgery (37 percent as compared with 60–84 percent).[5] All patients were encouraged to take deep breaths and to cough during the early postoperative period. No patient required re-intubation and ventilation for respiratory complications.

Safety. Geographically, the general recovery ward is ideally suited to cope with life threatening complications. It is part of the theatre complex and is adequately staffed with nursing and medical personnel over the 24-hour period. It is also within easy reach of the intensive care unit. Such complications as there were few, and were successfully managed. Equipment for cardiopulmonary resuscitation, ventilation and thoracotomy was, in any case, standard in this area.

References

1. Hutter JA, Aps C, Hemsi D, Williams BT. The management of cardiac surgical patients in a general surgical recovery ward. *Journal of Cardiovascular Surgery* 1986 (in press).
2. Kesteven PJ, Aps C, Williams BT, Ahmed A, Savidge GP. Heparin reversal following cardiopulmonary bypass. *Journal of Cardiovascular* 1986 (in press).
3. Noback C, Tinker JH. Hypothermia after cardiopulmonary bypass in man: amelioration by nitroprusside-induced vasodilation during rewarming. *Anesthesiology* 1980; **53:** 277–80.
4. Crawford RD. Hypothermia after cardiopulmonary bypass in man. *Anesthesiology* 1982; **56:** 234.
5. Karis JH. Hypothermia after cardiopulmonary bypass in man. *Anesthesiology* 1982; **56:** 233.
6. Morel DR, Forster A, Suter PM. i.v. labetalol in the treatment of hypertension following coronary-artery surgery. *British Journal of Anaesthesia* 1982; **54:** 1191.
7. Marty J, Binoche T, Pandele G, Akrouf A, Farinotti R, Henzel C, Desmonts JM. Influence of pain relief and rewarming on post-anesthetic adrenergic responses. *Anesthesiology* 1983; **59:** A129.
8. Flynn PJ, Hughes R, Walton B. The use of atracurium in cardiopulmonary bypass with induced hypothermia. *Anesthesiology* 1983; **59:** A262.
9. Aps C, Inglis MS. Peritoneal closure and atracurium. *Anaesthesia* 1984; **39:** 187.
10. Taylor P. Are neuromuscular blocking agents more efficacious in pairs? *Anesthesiology* 1985; **63:** 1–3.
11. Reves MD, Fragen RJ, Vinik HR, Greenblatt BJ. Midazolam: pharmacology and uses. *Anesthesiology* 1985; **62:** 310–24.
12. Mirakhur RK, Dundee JW, Clarke RSJ. Glycopyrrolate–neostigmine mixture for antagonism of neuromuscular block: comparison with atropine-neostigmine mixture. *British Journal of Anaesthesia* 1977; **49:** 825–9.
13. Mirakhur RK, Dundee JW. Lack of anti-emetic of glycopyrrolate. *Anaesthesia* 1981; **36:** 819–20.
14. Caldwell CB, Gross JB. Physostigmine reversal of midazolam-induced sedation. *Anesthesiology* 1982; **57:** 125–7.
15. Gale GD, Teasdale SJ, Sanders DE, Bradwell PJ, Russell A, Solaric B, York JE. Pulmonary atelectasis and other respiratory complications after cardiopulmonary bypass and investigation of aetiological factors. *Canadian Anaesthetists' Society Journal* 1979; **26:** 15–21.

Anaesthesia, 1986, Volume 41, pages 537–541

Morbidity after day case laparoscopy. A comparison of two techniques of tracheal anaesthesia

M. Skacel, BSc, MB, BS, Registrar, P. Sengupta, MB, BS, MRCP, FFARCS, Senior Registrar. O.M. Plantevin, MB, ChB, FFARCS, Consultant, Department of Anaesthesia, St Thomas' Hospital, London SE1.

Summary

A comparison was made of postoperative morbidity following two anaesthetic techniques for day case laparoscopies. One group of patients was allowed to breathe spontaneously after intubation under suxamethonium. The second group received atracurium and their lungs were mechanically ventilated. Patients in the controlled ventilation group experienced significantly less severe sore throats and muscle pain in the first 24 hours postoperatively than the patients who breathed spontaneously. Both techniques proved to be safe and are suitable for day case laparoscopy. The safety of patients is discussed in relation to the choice of anaesthetic technique used.

Key words
Anaesthesia; outpatient.
Neuromuscular relaxants; atracurium, suxamethonium.

Laparoscopy has been shown to be a safe procedure[1] with a high degree of patient acceptance.[2,3] However, symptomatic morbidity is high following any laparoscopy[2,4] and numerous investigations have been

---

Correspondence should be addressed to Dr O.M. Plantevin, please.

undertaken to elucidate which anaesthetic technique is best for this procedure. Opinion still recommends tracheal intubation in these patients; ventilation can be spontaneous or controlled. Both Heneghan *et al.*[5] and Kurer and Welch,[6] when examining outpatient dental and inpatient gynaecological surgery respectively, found that a spontaneously breathing technique produced less postoperative morbidity when compared with the controlled ventilation technique. The studies used alcuronium and pancuronium respectively as the neuromuscular blocking agent.

Recently Collins *et al.*[2] have shown that atracurium produces significantly less postoperative morbidity than alcuronium, presumably due to its shorter duration of action, and appears to be the muscle relaxant of choice in day case anaesthesia.

This study was designed to compare the postoperative morbidity of spontaneous respiration after intubation with suxamethonium and controlled ventilation with atracurium; all other drugs used were the same.

Method

Forty-six consecutive patients admitted for outpatient gynaecological laparoscopy were entered in the trial. Patients conformed to ASA grades 1 or 2 and were deemed suitable for day case surgery. The patients were assessed pre-operatively by the anaesthetist and informed consent obtained. They were then randomly allocated to one of two groups. No premedication was given. All anaesthetics were administered by either M.S. or P.S. and the same gynaecologist performed the laparoscopies.

All patients received metoclopramide 10 mg intravenously, fentanyl 1 μg/kg and a sleep dose of thiopentone via an indwelling needle inserted in the back of the hand, followed by either suxamethonium 1 mg/kg or atracurium 0.3 mg/kg. The trachea was intubated after the muscle fasciculations had ceased in the suxamethonium group and two minutes later in the atracurium group. Patients in the suxamethonium group were then allowed to breathe spontaneously using a semi-closed circle system with a fresh gas flow of 6 litres/minute (66 percent nitrous oxide/33 percent oxygen) to which enflurane 1.5–2.5 percent was added. The lungs of the patients in the atracurium group were mechanically ventilated using a Manley ventilator with a minute volume of 80 ml/kg (66 percent nitrous oxide/33 percent oxygen) plus enflurane 0.5 percent. At the end of surgery, the residual effects of atracurium were reversed with neostigmine 2.5 mg and atropine 1.2 mg. In both groups, the concentration of enflurane was increased or a small incremental dose of thiopentone given if indicated.

Once anaesthesia was induced, patients were placed in the lithotomy position, catheterised if necessary and 20° of head down tilt applied. Carbon dioxide was used as the insufflating gas and care was taken to expel as much gas as possible before the trocar was removed at the end of surgery. Heart rate and blood pressure were measured at the initial clinical assessment and the ECG was monitored continuously using a Cardiorator CR5 on standard lead 2. Pulse rate and arterial blood pressure were recorded every 5 minutes.

In the recovery room, trained nursing staff, who were unaware of which technique had been used, recorded the time for the patients to open their eyes to command, and the occurrence of nausea, vomiting, abdominal pain or other symptoms. All patients were then given three morbidity questionnaires to complete, one at discharge and the other two at 24 and 48 hours postoperatively.

Results were analysed using a Chi squared test for postoperative morbidity and Students *t*-test for pulse and arterial blood pressure recordings.

Results

There were 24 patients in the atracurium and 22 in the suxamethonium groups. One patient in the latter was not included in the results because of language difficulties, and four patients did not return the questionnaires, one in the atracurium group and three in the suxamethonium group. There was no significant difference between the groups in age, weight, pre-operative blood pressure, pre-operative heart rate or duration of anaesthesia. (Table 1).

Both techniques provided good cardiovascular stability during the procedure. There was no difference statistically between the peroperative maximum heart rates of the atracurium or suxamethonium groups,

Table 1. Patient data

	Suxamethonium group ($n = 18$)	Atracurium group ($n = 23$)
Age (years, SEM)	31.4 (1.2)	29.5 (1.5)*
Weight (kg, SEM)	63.5 (2.4)	61.7 (1.3)*
Pre-operative		
Heart rate (bpm, SEM)	79.0 (2.3)	79.1 (2.0)*
Systolic blood pressure (mmHg, SEM)	112.0 (2.2)	113.0 (1.9)*
Duration of anaesthesia (minutes, SEM)	20.5 (4.1)	19.8 (3.8)*

*, Not significant at the $p = 0.05$ level.

which were 85 (SEM 2.1) beats/minute and 86 (SEM 2.5) beats/minute respectively. There was no difference between the groups as regards blood pressures at any stage of the procedure. Two patients had dysrhythmias during surgery, a bradycardia of less than 40 beats/minute, which was treated with atropine, and a self limiting episode of ventricular bigeminy. Both these were in patients of the atracurium group. This was not statistically significant.

During surgery, 14 patients in the atracurium group required the enflurane concentration to be increased to 1 percent, and of these one needed a further dose of thiopentone (100 mg). In the suxamethonium group, seven patients required further thiopentone (50–150 mg), and one of these needed a further dose of suxamethonium (25 mg). The mean recovery time was 3.5 minutes (range 1–10) in the atracurium group and 5 minutes (range 1–13) in the suxamethonium group. This was not statistically significant. Three patients required pethidine for postoperative pain relief, one in the suxamethonium group and two in the atracurium group. There was no difference in the immediate postoperative morbidity (Table 2), apart from the fact that ten patients in the atracurium group experienced dreams; none of these was unpleasant or appeared to be related to the procedure.

Table 2. Number of patients experiencing symptoms immediately prior to discharge

Symptoms	Suxamethonium group ($n = 18$)	Atracurium group ($n = 23$)
Headache	4	4*
Sore throat	15	19*
Nausea	11	10*
Vomiting	7	7*
Dizziness	9	14*
Dry mouth	9	18*
Double vision	3	5*
Backache	4	4*
Abdominal pain	18	22*
Other pains	6	7*
Dreams	0	10 ($p < 0.01$)

*, Not significant at the $p = 0.05$ level.

The morbidity at 24 hours postoperatively is shown in Table 3. The severity, but not the incidence, of neck and shoulder pain and sore throats was significantly higher in the suxamethonium group. The analgesic requirements of the patients in this group was also increased in the first 24 hours. There was no difference in the incidence or severity of headache, abdominal pain, rib pain, backache, and nausea or other sequelae. At 48 hours postoperatively, there was no difference in any index of morbidity or analgesia usage.

All patients experienced some symptoms in the first 24 hours. Seven patients (38.8 percent) in the suxamethonium group and six (26 percent) in the atracurium group would have preferred the procedure as inpatients. Sixteen patients in the atracurium group and 14 in the suxamethonium group would like to have the same anaesthetic again. The majority of patients who did not want the same general anaesthetic stated that they had previously had inpatient surgery and compared that experience to this present one.

Discussion

Outpatient laparoscopy is increasingly practised for social and economic reasons. Previous studies have shown that this type of surgery meets with a high degree of patient acceptance, and only 30 percent of the patients in the studies by Collins *et al.*[2] and Kurer and Welch[6] would retrospectively have preferred to be inpatients. This is in accord with our study, where 31 percent of patients would have preferred to be inpatients.

However, symptomatic morbidity is known to be high following this procedure[2,4] and therefore, any anaesthetic technique which reduces the incidence

Table 3. Number of patients experiencing symptoms at 24 hours postoperatively

Symptom	Suxamethonium group ($n = 18$)	Atracurium group ($n = 23$)
Neck and shoulder pain		
none	5	4
slight	3	12
moderate	2	4
severe	8	3
	$p < 0.05$	
Sore throat		
none	3	15
slight	5	4
moderate	7	2
severe	3	2
	$p < 0.05$	
Analgesic use (number of times two tablets of aspirin used in first 24 hours)		
none	0	4
once	3	10
twice	7	3
three or more	8	6
	$p < 0.05$	

or severity of the sequelae would be advantageous to the patient. Anaesthetic opinion at the moment still recommends tracheal intubation for this procedure, to prevent complications arising either from gastric regurgitation due to the Trendelenberg tilt, or respiratory insufficiency in the presence of a raised intra-abdominal pressure due to the carbon dioxide pneumoperitoneum. Controlled ventilation has been advocated by Scott and Julian,[7] because of a high incidence of dysrhythmias in patients breathing spontaneously with halothane, although, Harris *et al.*[9] have shown no difference in the incidence of dysrhythmias in patients breathing spontaneously when enflurane was used.

Recently, both Heneghan *et al.*[5] in day case dental surgery and Kurer and Welch[6] in inpatient laparoscopies have shown that a spontaneous breathing technique using suxamethonium to facilitate intubation, produced less postoperative morbidity than a controlled ventilation technique using alcuronium and pancuronium respectively. A significant proportion of the sequelae quoted in the above studies consisted of blurred or double vision, general weakness and muscle pain. Collins *et al.*[2] found that atracurium was associated with significantly less morbidity than alcuronium and postulated that the longer duration of neuromuscular blockade caused incoordination and subsequent muscle strain. Controlled ventilation with atracurium should therefore produce less postoperative morbidity than other nondepolarising relaxants and might be superior to spontaneous ventilation after intubation under suxamethonium. All patients received the same dose of metoclopramide and fentanyl, and enflurane was used in both groups as the inhalational agent. In this way, it was hoped that any differences in postoperative morbidity would be attributable to the different techniques of neuromuscular paralysis.

Although in our study we found a similar incidence of postoperative symptoms, neck and shoulder pain was significantly less severe in the atracurium group than in patients who had received suxamethonium. The incidence of muscle pain after suxamethonium and early ambulation is well documented and is believed to be due to muscle fasciculations. In this study we did not pretreat our patients with a small dose of a non-depolarising agent. This may have reduced the severity and incidence of neck and shoulder pain, although Frew *et al.*[9] in their study of outpatient laparoscopies found that the incidence and severity of neck and shoulder pain was not reduced by pretreatment with gallamine.

Sore throat is associated with the presence of a tracheal tube and the higher incidence in patients breathing spontaneously was not unexpected. This is probably due to the vocal cords tightening around the tracheal tube after recovery from suxamethonium, thus causing more movement of the tube against the larynx. The incidence of sore throats may be reduced by avoiding tracheal intubation, although Kurer and Welch[6] found no difference in the incidence of sore throats at 24 hours postoperatively when a spontaneous breathing technique using a face mask was compared to controlled ventilation with pancuronium.

The increased morbidity of the suxamethonium group of patients was accompanied by the fact that this group of patients also required more oral analgesia in the first 24 hours. Just prior to discharge the only difference in morbidity was in the incidence of dreams. Ten patients (45 percent) in the atracurium group experienced dreams, none of which was unpleasant or appeared related to the procedure, while no patient in the suxamethonium group could recall having one. The probable explanation is that the atracurium group were not as deeply anaesthetised and indeed, the anaesthetist considered that in 14 patients the enflurane concentration needed to be increased.

Both techniques provided good cardiovascular stability and a low incidence of dysrhythmias, unlike Kurer and Welch[6] who found an 18 percent and 5 percent incidence of dysrhythmias in the spontaneous ventilation and controlled ventilation groups respectively, when halothane was used as the inhalational agent. Recently, Harris *et al.*[8] have shown no difference in the incidence of dysrhythmias between the above techniques when enflurane was used.

Whilst postoperative morbidity is of importance, the safety of the patient obviously influences the choice of anaesthetic technique. Tracheal intubation[2-4,10,11] has been used to prevent inhalation of gastric contents, but Kurer and Welch[6] found no evidence of passive regurgitation during laparoscopies that lasted 5 minutes with a 10° Trendelenberg tilt. However, Duffy[11] found this a problem in patients undergoing laparoscopy in the 'lithotomy position and steep head-down tilt'. It may be that passive regurgitation would have proved more of a problem for Kurer and Welch if their laparoscopies had been of longer duration. Interestingly, 23 percent of their patients who breathed spontaneously through a facemask also developed airway problems. Therefore, the degree of Trendelenberg tilt, the skill of the anaesthetist and surgeon and the duration of laparoscopy must influence the choice of anaesthetic technique.

In summary, spontaneous ventilation using enflurane may be an advantage for short procedures because reversal of neuromuscular block will not be required, but this unfortunately is at the expense of an increased severity of sore throat and muscle pain. Controlled ventilation with atracurium may be the technique of choice for long procedures, or if steep Trendelenberg tilt is necessary; this also leads to less severe postoperative sequelae, but has an increased risk of awareness.

Acknowledgments

We should like to thank the staff of the Outpatient Theatres for their co-operation and help, particularly the recovery nurses and Miss S. Leitch.

References

1. CHAMBERLAIN G, CARRON-BROWN JA. Gynaecological laparoscopy—Report of the working party of the Confidential Enquiry into Gynaecological Laparoscopy. 1978.
2. COLLINS KM, PLANTEVIN OM, DOCHERTY PW. Comparison of atracurium and alcuronium in day-case gynaecological surgery. *Anaesthesia* 1984; **39:** 1130–4.
3. COLLINS KM, DOCHERTY PW, PLANTEVIN OM. Postoperative morbidity following gynaecological outpatient laparoscopy. A reappraisal of the service. *Anaesthesia* 1984; **39:** 819–22.
4. HARVEY DC, CHARLTON AJ, FINDLEY IL. Comparison of morbidity between inpatients and outpatients following gynaecological laparoscopy. *Annals of the Royal College of Surgeons of England* 1985; **67:** 103–4.
5. HENEGHAN C, MCAULIFFE R, THOMAS D, RADFORD D. Morbidity after outpatient anaesthesia. A comparison of two techniques of endotracheal anaesthesia for dental surgery. *Anaesthesia* 1981; **36:** 4–9.
6. KURER FC, WELCH DB. Gynaecological laproscopy: clinical experiences of two anaesthetic techniques. *British Journal of Anaesthesia* 1984; **56:** 1207–11.
7. SCOTT DB, JULIAN DG. Observations of cardiac arrhythmias during laparoscopy. *British Medical Journal* 1972; **1:** 411–3.
8. HARRIS MNE, PLANTEVIN OM, CROWTHER A. Cardiac arrhythmias during anaesthesia for laparoscopy. *British Journal of Anaesthesia* 1984; **56:** 1213–17.
9. FREW RM. HUTCHINSON R, KWIK R, WALTERS H, WILLIAMS TR. The avoidance of suxamethonium pains: a study of patients presenting for laparoscopy. *Anaesthesia* 1976; **31:** 97–106.
10. HODGSON C, MCCLELLAND RMA, NEWTON JR. Some effects of the peritoneal insufflation of carbon dioxide at laparoscopy. *Anaesthesia* 1970; **25:** 382–90.
11. DUFFY BL. Regurgitation during pelvic laparoscopy. *British Journal of Anaesthesia* 1979; **51:** 1089–90.

Anaesthesia, 1986, Volume 41, pages 541–543

Bromazepam as oral premedication. A comparison with lorazepam

R. Ponnudurai, FFARCS, Registrar, J. Hurdley, FFARCS, Consultant, Anaesthetic Department,
Selly Oak Hospital, Birmingham B29 6JD.

Summary

A double-blind trial of bromazepam 6 mg versus lorazepam 2 mg as oral premedicant agents was undertaken. A total of 153 patients were studied; 78 received bromazepam and 75 lorazepam. Objective and subjective assessments of sedation, amnesia, nausea and vomiting were performed. No significant difference between the two groups was found. It was concluded that bromazepam 6 mg and lorazepam 2 mg were equally satisfactory as premedicant drugs.

Key words

Hypnotics, benzodiazepines; bromazepam, lorazepam.

Bromazepam is a recently introduced benzodiazepine with sedative and anxiolytic properties. It has been shown to be superior to diazepam in its anxiolytic effect in psychiatric patients.[1] Orally it has a peak effect in 1–4 hours and a half life of 11.9 hours.

Lorazepam has been shown in a number of studies to be a satisfactory premedicant drug when given orally approximately 2 hours pre-operatively.[2–4] Its duration of action is such that the timing of the dose is not critical. We have had reports from the ward staff, however, of a small proportion of patients who have vomited immediately after receiving lorazepam orally, thereby rendering it ineffective.

A double-blind study of the two drugs as oral premedicants was undertaken.

Correspondence should be addressed to: Dr. J. Hurdley, Anaesthetics Department, Selly Oak Hospital, Birmingham, B29 6JD.

Method

The study was approved by the South Birmingham district ethical committee. Patients were selected from a gynaecology ward, who were due to be operated on by the same surgical team. All types of gynaecological surgery were included, but patients with co-existing disease requiring drug therapy, those receiving psychoactive drugs or night sedation were not studied. All observations were made by the same author.

Patients were assessed the day before surgery for their anxiety level (Table 1), pulse rate and arterial blood pressure. They were shown three picture cards (from a set of 20) of common objects and asked to remember them. They were randomly allocated to two groups. At 12.00 hours on the day of surgery, they were given orally a coded capsule containing either bromazepam 6.0 mg or lorazepam 2.0 mg. In the anaesthetic room anxiety level was assessed and pulse rate and blood pressure measured. The patients were asked to recall the pictures they had been shown, and also whether they had experienced nausea or vomiting. After venepuncture, pulse rate and arterial blood pressure were measured again.

The following day the patients were visited and the recall of the picture cards tested. Enquiries were made into the presence or absence of postoperative nausea or vomiting. Sedation scores out of 10 were awarded according to the method of Nisbet and Norris;[5] a high score indicated a high level of sedation (Table 1).

Results

There were 153 patients in the study, 78 in the bromazepam group and 75 in the lorazepam group. The groups were comparable in terms of age distribution and weight (Table 2). There was no significant difference in sedation scores between the two groups as tested by Chi squared (Table 3). No differences were found in the incidence of nausea, vomiting or amnesia, although there was less vomiting in the bromazepam group (Table 4).

Table 1. Subjective and objective scoring method

Subjective	
A. Subjective state in anaesthetic room	
Apprehensive	0
Fully awake	1
Drowsy	2
B. Change in state from ward to anaesthetic room	
Apparent improvement	2
No change	1
Apparent deterioration	0
Objective	
A. Change from ward to anaesthetic room	
Fall in systolic blood pressure >10 mmHg	2
No change	1
Rise in systolic blood pressure >10 mmHg	0
Fall in heart rate >10 mmHg	2
No change	1
Rise in heart rate >10 mmHg	0
B. After stimulation (venepuncture)	
Rise in systolic blood pressure >10 mmHg	0
No change	1
Rise in heart rate >10 mmHg	0
No change	1

Any degree of failure to recall the picture cards was recorded as amnesia.

Table 2. Distribution of patients by treatment, age and weight

	Bromazepam 6 mg	Lorazepam 2 mg	
Age (years)			Total
0–24	4	7	11
25–44	55	40	95
45–64	18	27	45
>65	1	1	2
Total	78	75	153
Weight kg	63.7	61.57	
SEM ($p = 0.26$)	1.3	1.4	

Discussion

Nisbet and Norris[5] defined a score of 4 or less as being poor sedation and a score of 7–10 as being good. Only eight patients had a score of 4 or less, while 89 had scores of 7 or more. The sedation achieved with bromazepam is not significantly different from that with lorazepam, although comments from patients who were known to have had lorazepam outside the study

Table 3. Distribution of patients by treatment and sedation score

Score	Bromazepam 6 mg	Lorazepam 2 mg
3	2	1
4	3	2
5	8	7
6	21	20
7	19	21
8	20	17
9	4	6
10	1	1
Mean	6.7	6.8

A Chi squared test on the two treatment groups gave a p value of greater than 0.1.

Table 4. Distribution of patients by treatment and unsolicited side effects

Effect	Bromazepam 6 mg	Lorazepam 2 mg
Nausea		
Same day	3	0
Next day	13	17
Vomiting		
Same day	0	0
Next day	3	6
Amnesia		
Same day	4	6
Next day	1	1

The terms 'Same day' and 'Next day' refer to the time of questioning so 'Same day' means pre-operative and 'Next day' postoperative. A Chi squared test of the incidence of nausea and vomiting between the groups gives $0.5 > p > 0.2$.

indicate that there may be a subjective difference in the sedation caused by the drugs. There was no significant difference between the groups in terms of the incidence of nausea or vomiting and there was no record of any patient vomiting immediately after receiving either drug. Particular note of this had been made, in view of the reports from ward staff before the trial. The overall incidence of vomiting was 5.9 percent, which we thought surprisingly low.

The test of amnesia was designed to be as objective as possible and there was no difference between the drugs in this respect. Amnesia is not an undesirable side effect in the context of premedication and patients do not find it unpleasant.

Some studies have found lorazepam to be superior to diazepam as a premedicant,[3] others have found no difference.[2] A recent study of bromazepam versus diazepam showed no significant difference between these two drugs.[6]

We would conclude that bromazepam 6 mg and lorazepam 2 mg are equally satisfactory when used as oral premedication.

Acknowledgments

The authors gratefully acknowledge the help of Dr Nutley and Miss Payne of Roche Products in preparing this study and for the supply of coded capsules of the two drugs. We thank Mrs S. Roden and the Pharmacy Department of Selly Oak Hospital for supervising the coding and premedication of the patients and Dr T.B. Strain, consultant anaesthetist for help with the trial. The patients were admitted under the care of Mr J.R. Pogmore, MRCOG whom we thank for his patience and cooperation.

References

1. Fontaine R, Annabel L, Chouinard G, Ogilvie RI. Bromazepam and diazepam in generalized anxiety: a placebo controlled study with measurement of drug plasma concentrations. *Journal of Clinical Psychopharmacology* 1983; **3:** 80–7.
2. Paymaster NJ. Lorazepam (WY 4036) as a pre-operative medication. *Anaesthesia* 1973; **28:** 521–6.
3. Cremonesi E, da Silva LFN, Curras JS, Antunes AHC, Moraes R, Sartoretto JN. Evaluation of lorazepam as an oral preanaesthetic medication. A comparative double blind study with diazepam and placebo. *Current Medical Research and Opinion* 1974; **2:** 244–8.
4. Loach A, Fisher A. Lorazepam as a premedicant for day-case surgery: an assessment. *Anaesthesia* 1975; **30:** 545–9.
5. Nisbet HIA, Norris W. Objective measurement of sedation II: A simple scoring system. *British Journal of Anaesthesia* 1963; **35:** 618–23.
6. Chalmers P, Horton JN. Oral bromazepam in premedication. A comparison with diazepam. *Anaesthesia* 1984; **39:** 370–2.

Anaesthesia, 1986, Volume 41, pages 543–546

Fire in the operating theatre. Evacuation pre-planning may save lives

Mary A. Moxon, MB, ChB, FFARCS, Senior Registrar, Royal Berkshire Hospital, Reading, M.E. Ward, MB, BS, FFARCS, Consultant Anaesthetist, Nuffield Department of Anaesthetics, John Radcliffe Hospital, Headington, Oxford, OX3 9DU.

Summary

An operating theatre fire and the steps taken to deal with it are described; the difficulties encountered in evacuating anaesthetised patients are highlighted. Measures which might be taken to prevent recurrence of these problems, and recommendations on the institution of fire drills for the safety of patients and staff are given.

Key words
Operating rooms; personnel.
Electrical systems; fire.

Fires occur in hospitals, as in other occupied buildings with surprising frequency; 2212 were reported to the Home Office by the Fire Research Station in 1982. Most of these fires are not serious and are quickly brought

---

Correspondence should be addressed to Dr M.E. Ward please.

under control, with no risk to patients or staff. Fire in a hospital is potentially serious not only because of extensive damage to property, but because evacuation of patients may be involved. The hazards may be further increased if patients are unable to help themselves due to mental or physical infirmity.

Fire in operating suites is relatively rare but potentially particularly dangerous. The hazards in modern operating theatres are increased by the proximity of electrical equipment to anaesthetic gases which may support combustion or be inflammable. An anaesthetised patient is totally dependent; if surgery is in progress, evacuation may be a serious risk to life.

Description of fire

We report a minor fire in the operating suite, in which two anaesthetised patients and another recovering from anaesthesia and surgery had to be evacuated, and describe the problems that were encountered.

The suite has four theatres, of which only two were being used—one for plastic surgery and one for neurosurgery (Fig. 1). There was also a patient in the recovery area. The plastic surgery (cross-face nerve graft) had been underway for over an hour, the patient was paralysed and receiving controlled ventilation of the lungs, the surgery involved a microvascular anastomosis and to facilitate this a hypotensive technique was being used. The neurosurgical patient was in the anaesthetic room and had just been anaesthetised prior to a posterior craniotomy. The patient in the recovery area had already undergone surgery and had been there for 10 minutes.

The first sign of any hazard was when some lights and power sockets failed, but the operating lights remained on. The electricians were notified since the emergency generator did not take over. The neurosurgical case was moved into theatre and onto the operating table so that preparation for surgery could continue. About 8–10 minutes after the partial power failure, dense smoke was seen in the corridor behind the neurosurgical theatre and the patient was moved back onto a trolley to the reception area and kept anaesthetised and ventilated with an Ambu Bag supplied by a cylinder of Entonox. It was fortunate that, as the operating tables are non-mobile, the customary fixation of the patient's head to the operating table with three pins had not been done.

The plastic surgery patient was also moved to the reception area and anaesthesia maintained with nitrous oxide and oxygen from a Boyle's machine supplied by cylinders. The patient was ventilated using a Nuffield ventilator powered by a cylinder of oxygen. The open wound was packed with swabs. The patient in recovery was also moved into this area. The electricity supply to the entire suite was then switched off by the engineer. An alternative non-mains supply of light, such as torches, could not be found, so evacuation was undertaken to the adjacent corridor outside the sterile area

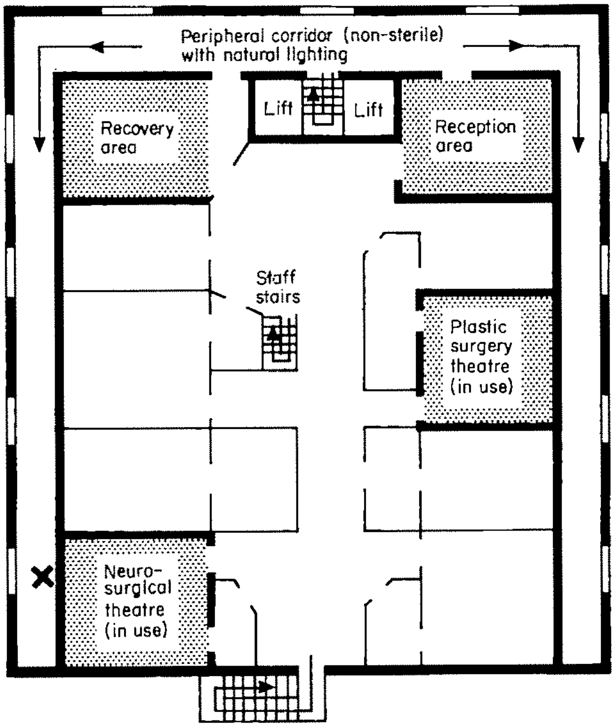

Peripheral corridor (non-sterile) with natural lighting
Lift
Lift
Recovery area
Reception area
Staff stairs
Plastic surgery theatre (in use)
Neuro-surgical theatre (in use)
×
External fire escape

Fig. 1. Plan of third floor theatres. Source of smoke shown by x.

where there are windows and some natural light. The fire brigade had arrived by this time and entered the theatre suite—in the interest of speed they were not required to wear theatre clothing. It was decided to awaken the neurosurgical patient, but further problems and delays were encountered because non-electrical suckers were not available in the theatre block and an Ambu foot-sucker had to be brought from another part of the hospital.

The fire was soon brought under control by the local fire service who reported that the smoke was in fact due to an electrical fault in a junction box which had been overloaded (Fig. 2). The patient undergoing facial nerve graft was taken back into the theatre furthest from the source of the smoke. The rest of the suite was not used for about an hour, to allow the smoke to disperse.

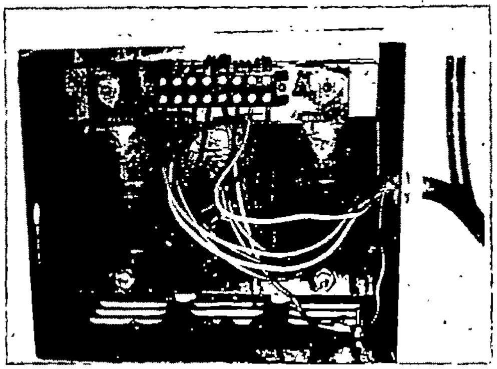


Fig. 2. Overloaded and smoke blackened electrical junction box.

Subsequently, the fault was found to be overheating in the transformer supplying the Maquet table motor, causing a single fuse to blow downstream of the generator. This meant that the sensory electrical circuits which should have detected the broken circuit had not done so, thus preventing the emergency generator from being switched into the power supply.

The theatre suite is located on the third floor of a modern building (opened 10 March 1972) which also houses the neurosurgical intensive care unit, one floor below. Apart from the lifts, there is a narrow staircase for staff and an external fire escape which is also very narrow. There are *no* automatic fire or smoke devices in the theatre! Lateral evacuation is possible only to the narrow corridor outside the theatre suite (see Fig. 1).

All the staff coped very well when faced with the emergency, but there was no obvious 'drill' procedure upon which to act. The deficiencies in equipment for such an emergency were lack of a non-mains light source and non-electrical suckers. Further problems would obviously have arisen if the neurosurgical case had actually started and there had been a need to evacuate either this case, or the patient who was deliberately hypotensive having been given ganglion blocking agents, down the stairs or fire escape.

Table 1. Fires in hospitals in the United Kingdom attended by the Fire Brigade. (Source: returns by fire brigades to Home Office and Fire Research Station.)

	Number	Number of fire-related	
Year	of fires	Deaths	Injuries
1971	1349*	12	20
1972	1639*	41†	71
1973	2044	15	52
1974	2047	13	48
1975	2200‡	7	N.A.
1976	2219	7	47
1977	2148§	9	50
1978	1878§	9	59
1979	2055	20	92
1980	2106§	3	84
1981	2081	18	68
1982	2212	7	70

*The lower level of these figures is attributable to lower reporting of fires to fire brigades rather than fewer actual fires in hospitals in these years.

†Includes 30 at one incident—Coldharbour Hospital, Sherbourne.

‡Estimated figure.

NA Not available.

§These figures are lower than expected because of non-reporting by fire brigades during periods of industrial action by firemen.

Discussion

Fire remains a serious hazard in any occupied building and the number of fires is not decreasing, as can be seen from Table 1. Death and injuries do still occur, despite our increasing awareness and improved standards of fire precautions. Fires in operating suites comprise a very small proportion of all hospital fires. Fifteen out of a total of 7078 in 1971–84,[1] 3 out of a total of 949 in the South East Thames Region in 1979–82.[2] However, they are potentially very serious. It would seem essential, therefore, to have an evacuation plan which all the staff have studied or practised, as well as basic equipment which does not rely on mains electricity or piped gas in order to function.

Regular fire drills may not be practical, as they may interrupt work and endanger sterility; however, a one-off practice, undertaken with the help of the hospital fire officer and local fire brigade, and involving substitute patients, would highlight problems. These could then be eliminated at leisure. This type of drill was reported by Nagel and others in 1973 in the USA and was seen to work well.[3] A simple guide to fire drill and evacuation procedures could then be drawn up and issued as essential reading to all new theatre staff. Each member of staff would then be expected to know his/her specific task in the event of an emergency and be questioned on it as part of theatre training.

The medical staff present have to make the final decision regarding the care and type of handling of each patient in such an emergency, but it is important that all the staff understand the guidelines and principles involved so that there is a minimum of explanation necessary and vital minutes are not lost.

Furthermore, the execution of the evacuation plan may need to take place in a smoke-filled, dark and noisy environment. The plan should recognise the need to maintain intravenous lines, the need to continue oxygen therapy or artificial ventilation and should also include details of staff needed to move patients. If surgery is in progress, advice should be available on when to interrupt or terminate the procedure most safely for the patient and staff.[4] Whilst it is not possible to imagine every eventuality in each theatre suite, those sited above ground or first floor level, where evacuation would be difficult, should make special plans for a drill which can be put into practice occasionally, to make sure it is realistic and adaptable enough to cover most emergency situations.

The importance of regular maintenance of gas pipelines, cylinders, and electrical equipment cannot be overstressed. It is also important that vital life-dependent and monitoring equipment is available which can be powered by batteries; these should be checked regularly. In addition, staff must be encouraged to report any fault they find with equipment as soon as possible, so that checks can be carried out. Even a small electrical fault can cause a major fire.

Conclusion

Fire is a rare event in an operating suite. However, it can be disastrous and the 'it will never happen to me' syndrome should not be allowed to creep in. All staff should understand the potential hazards of equipment in use in a theatre suite and refuse to use equipment if it is faulty or has not been checked.

Although these points are important, prevention can never be complete and it is essential that there is a fire drill which takes into account all the likely problems. Theatre staff must be conversant with the drill and put it into practice from time to time. Fire practices are a bore for some and a distraction for others but, for the safety of staff and the patients in their care, the occasional disruption of a theatre list and dirtying of a sterile area cannot be weighed against the possibility of unnecessary risks and possible loss of life.

The DHSS expects Health Authorities to have clearly defined policies for preventing fires and procedures for dealing with their outbreak in health care premises. General guidance on the role of management in devising and implementing policies and plans for dealing with the threat posed by fire, and for ensuring that all staff receive appropriate training in fire safety, is given in HTM83, 'General Fire Precautions'. Specific guidance in developing fire policies and plans is given to Authorities in the document entitled 'Fire Precautions Development Programme' (Section 1). These should be available in every hospital.

References

1. Chandler SE. Some trends in hospital fire statistics. Building Research Establishment. Current Paper November 1978.
2. Rees DG. Department Health and Social Security (personal communication).
3. Nagel EL, Perdue M, Hayes JD, Kennedy N. Drill prepares OR for fire emergency. *Hospitals* 1970; **47**: 99–105.
4. Farman JV. Safety of the Surgical Patient. *Proceedings of The Royal Society of Medicine* 1978; **69**: 603–4.

Anaesthesia, 1986, Volume 41, pages 547–561

Correspondence

Legal standard wire gauge 547
M.E. Davis, MB, BS
Kappa agonists in anaesthesia 549
R. Simionescu, MD
A possible case of red rubber sensitivity 549
H.M. Basavaraja, MB, BS, S. Firn, FFARCS and J. Watkins, PhD
Cross-reactions of neuromuscular blocking, drugs and anaphylactoid reactions 550
B.A. Baldo, PhD
Neuroleptic malignant syndrome 551
J.W. Mackenzie, MRCP
Anne E. Peebles-Brown, FFARCS
Crystalloids are alive and well 551
R.A. Cajee, FFA(SA), and E.B. Furman, FFA(SA)
K.M. Hillman, FFARCS 552
Epidural analgesia in the presence of fever 553
D.G. Thomas, FFARCS
Priming volume of epidural equipment 554
J. Oyston, MB, BS
Bradycardia and hypotension in spinal anaesthesia 554
C. McLoughlin, MB, BCh
Generalised oedema and epidural analgesia 554
J. Gardiner, FFARCS
Stability of diamorphine-sodium chloride solutions 554
Felicity Reynolds, MD, FFARCS
An unusual complication using a 'Butterfly' needle 555
A.P. White, MB, BS
F.E. Bennetts, FFARCS 556
Pain in the orbit: a feature of dural tap 556
C.M. Kumar, DTCD, FFARCS and B. Dennison, FFARCS
Mask for child resuscitation 557
M. Yamashita, MD and K. Motokawa, MD
An unusual epidural needle 557
S.M. Mostafa, FFARCS
Nosworthy anaesthetic record 558
P.H.P. Harris, FFARCS
Hazards with a Mediplast Coax 2 system 558
J.E. Sweeney, FFARCS
G. Cranstone 558
An improved pressure infusor 558
D.R. Goldhill, FFARCS, T.J. Dines, A.J. Clark
Multiple cannulation of a single vein 559
I.P. Latto, FFARCS and P.J. Hilton, FFARCS
External jugular vein catheterisation 560
P. Bouju, MD, H. Dreux-Boucard, MD, J.-F. Amiot, MD and J.H. Palacci, MD
A simple aid to central vein cannulation 560
A. MacNeil, FFARCS
Another aid for the insertion of nasogastric tubes 561
C.M. Kumar, DTCD, FFARCS
Evaluation of Ivac 560 volumetric pump 561
D.B. Revell

Legal standard wire gauge

Arbitrary gauges continue to be used despite metrication. Full metrication for hypodermic injection needles is feasible and could simplify the present system of dual numbering. The purpose of this memorandum is to discuss the actual gauge sizes or external diameters of injection needles in relation to the designated sizes as given by the Standard Wire Gauge or G numbers.

The diameters of wires have been expressed by a variety of wire gauges for over a century and a half. It is not surprising that a wire gauge has come to be used

---

All correspondence should be addressed to Dr J.N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

Letters must be typewritten on one side of the paper and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters contained in 'Notice to Contributors' to *Anaesthesia* printed at the back of each issue. The degrees and diplomas of each author must be given in a covering letter.

Correspondence presented in any other style or format may be the subject of considerable delay and may be returned to the author for revision.

for the description of the diameters of injection needles which are fine tubes with wire-like dimensions. The two independent characteristics of an injection needle are its length and external diameter; the latter corresponds to the equivalent standard wire gauge size. Wall thickness, and hence internal diameter, is another characteristic of a needle. The wall thickness is determined by considerations of the strength of the material used in manufacture of the needle. The standard wire gauge is an arbitrary scale,[1] so the writer asked himself why the higher numbers refer to more narrow gauge needles and the lower G numbers the wider gauge needles. For example:

Hypodermic injection needles

Descriptive numbers	18G	19G	21G	23G
External diameters (millimetres)	1.2	1.0	0.8	0.6

The reason for this inverse relationship between descriptive numbers and external diameters is historical. In the nineteenth century, in commerce, the sizes of wire were estimated by certain more or less recognised standard wire gauges. The most commonly quoted was the Birmingham Wire Gauge also known as Stub's Iron Wire Gauge. This gave forty measurements which bore no definite relationship to each other ranging from the largest, Number 0000 = 0.454 inch to the smallest, Number 36 = 0.004 inch; Number 1 was 0.300 inch. A simple workshop Birmingham Wire Gauge instrument commonly used for measuring consisted of a piece of machined steel with appropriate gauge apertures at the periphery. Descriptive G numbers, not sizes, were used for identification on such notched gauges.

Sir Joseph Whitworth, one of whose contributions to engineering was standardisation at a time when parts of machines were not interchangeable and screw threads and sizes were only used by one firm or workshop, recognised and vigorously advocated the advantages of standardisation. In 1857, Sir Joseph, by then of Manchester, proposed a standard wire gauge which came to be generally recognised at a period when other arbitrary wire gauges tended to add to the general confusion. The Lancashire Gauge, for example, used as nomenclature the letters of the alphabet in addition to the numerals up to 80 for expressing the sizes of steel wire. Sir Joseph Whitworth's gauge ranged from one thousandth of an inch to half an inch by regular gradations of one thousandth.[2] Thus No. 1, the smallest, was 0.001 inch and No. 500 was 0.500 inch.

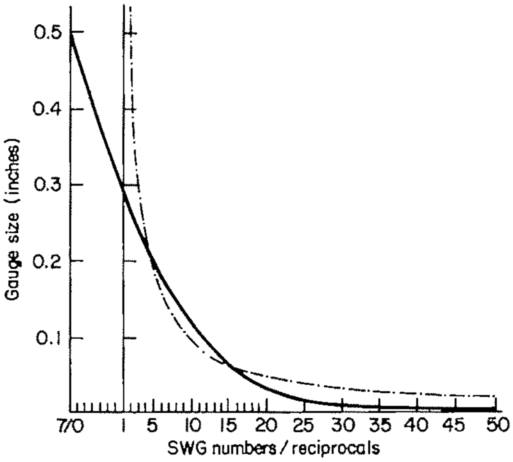


Fig. 1. Gauge size (inches) plotted against SWG numbers and reciprocals of G numbers. ——, G numbers; —·—, G numbers/reciprocals.

In Great Britain, one wire gauge has been legalised. This is the one we now refer to as the Standard Wire Gauge.[3] It apparently embodies features of the Birmingham Wire Gauge and the Whitworth Decimal Gauge in thousandths of an inch. Like the then well-known Birmingham Wire Gauge, there is an inverse relationship between the descriptive G numbers and the actual gauge sizes. The main scale ranges from G1 which measures 0.300 inch to G50 which is 0.001 inch, and there are fifty simple G numbers. There are, in addition, seven larger sizes allowed for; the descriptive numbers are 1/0, 2/0 … 7/0. These range from 0.324 inch for 1/0 to 0.500 inch for 7/0.

The complete table of the Standard Wire Gauge is published.[4] At gauge 16, the actual gauge size in inches approximates to the reciprocal of the G number. Reciprocals of G numbers of injection needles of the size range commonly used by anaesthetists, have been utilised as a ready means of estimating the external diameters of such needles. The results, which are in inches, can of course be converted to millimetres by applying the factor, × 25.4. Figure 1 illustrates the relationship. The only wire gauge to be legalised in the United States of America by an Act of Congress is the Birmingham Wire Gauge (Stub's).[5] Clearly, arbitrary gauge numbers are not self-explanatory and, in industry, gauge numbers are now being discarded. However, until metrication is complete the Standard Wire Gauge will continue to be used and a knowledge of what is implied by the term is helpful to all who regularly refer to it in their daily work. Both longitudinal and diametrical dimensions of injection needles can be readily described in millimetres, so the term SWG will, surely, be consigned to history.

London Hospital,
Whitechapel,
London E1 1BB

M.E. Davis

References

1. Macintosh Sir R, Mushin WW, Epstein HG. *Physics for*

the anaesthetist, 3rd edn. Oxford London Edinburgh Melbourne: Blackwell Scientific Publications, 1963: 427–8.
2. ANONYMOUS. *Encyclopaedia Britannica* 9th edn. Edinburgh: Adam and Charles Black, 1888; 24: 615.
3. OLBERG E, JONES FD, HORTON HL. *Machinery's handbook*, 20th edn. New York: Industrial Press Inc., 1975: 471–2.
4. MACKROW C. *Naval architect's, shipbuilder's and marine engineer's pocket-book*. 5th edn. London: Crosby Lockwood and Son, 1892: 216.
5. Anonymous. *Kempe's engineer's year book*, 90th edn. London: Morgan-Grampian Book Publishing Co., Ltd., 1985: E6/1.

Kappa agonists in anaesthesia

There seems, in my experience, to be a considerable difference between anaesthetics based on mu-agonists and anaesthetics based on kappa-agonists in poor risk patients. For example, after an intravenous induction with a barbiturate, when fentanyl and nitrous oxide anaesthesia is used in ASA 4 and 5 patients, profound hypotension develops and some of the ASA 5 patients never awaken. Conversely, when diazepam is used, followed by pentazocine and nitrous oxide anaesthesia, there is no hypotension and even ASA 5 patients wake up although many, of course, die as a result of progression of their disease.

It is clear that in some of these high risk patients, the cardiovascular system is maintained as a result of a full stress response. Mu-agonist drugs, like opiates, may involve the same mechanisms which are concerned with the maintenance of blood pressure. They add nothing to those of endogenous endorphins which are already high. Naloxone, a pure mu-antagonist, has been used to counteract the so-called irreversible hypotension of shock. Kappa-agonist drugs provide satisfactory analgesia without involving the mechanisms which are connected with the maintenance of blood pressure. These drugs are also partial mu-antagonists, so they may be more suitable for high risk patients since they do not interfere with the natural stress reactions.

Bul. Pacii 158 ap. 70 sect. 6,
77 538 Bucharest,
Romania

R. SIMIONESCU

A possible case of red rubber sensitivity

A 54-year-old female patient who weighed 68 kg was admitted with peritonitis. She required an emergency laparotomy, drainage of diverticular abscess and transverse colostomy. She had a past history of asthma with no known allergies; her hypertension was controlled with pindolol and clopamide. She was nervous and emotionally distressed; her arterial blood pressure was 110/70 mmHg and her pulse rate was 84/minute. No abnormalities of the cardiovascular system and respiratory system were noted. She had received several uneventful general anaesthetics in the past. She did not smoke.

Anaesthesia was induced with thiopentone 250 mg and suxamethonium 75 mg. An 8.5 mm cuffed red rubber tracheal tube was inserted into the trachea. Anaesthesia was maintained with fentanyl 0.1 mg, nitrous oxide 70 percent, oxygen 30 percent, enflurane 1 percent and atracurium was used for muscle relaxation (30-mg bolus with 10-mg increments every 20 minutes). Automatic ventilation of the lungs was with a Manley ventilator with an inflation pressure of 2.45 kPa and a tidal volume of 600 ml. The electrocardiogram and arterial blood pressure were monitored.

Twenty minutes after induction, the patient developed sudden marked bronchospasm, which failed to respond either to a bolus of aminophylline 250 mg administered intravenously over 10 minutes or to hydrocortisone 100 mg intravenously. Aminophylline 250 mg and hydrocortisone 100 mg in 500 ml normal saline were then infused over 30 minutes. The ventilator tidal volume was increased to 800 ml and the inflation pressure to 3.48 kPa in an attempt to improve the ventilation and halothane was substituted for enflurane. Temporary manual ventilation confirmed marked airway resistance. Auscultation of the chest during the aminophylline infusion showed that despite marked generalised bronchospasm, there was a variable intensity in the bronchospasm within the lungs; that is, the spasm varied from side to side and in different areas on the same side.

Salbutamol 0.7 mg was then administered intravenously, diluted in water, over 15 minutes with no effect. Blood pressure and heart rate remained stable (110–130 mmHg systolic and 65–80/minute). The tracheal tube was slightly withdrawn to eliminate the chance that it was in contact with the carina: this also caused no improvement.

These clinical observations over a 40-minute period suggested that there was a local focus of irritation, within the respiratory tract, which was triggering histamine release; the obvious culprit was the red rubber tracheal tube. A Portex tracheal tube was substituted with dramatic improvement in the bronchospasm, which disappeared within 20 seconds.

This case raises many questions about exactly what precipitated the severe and persistent bronchospasm in a patient who was known to be asthmatic. Several of the drugs used are known to cause histamine release. The delay of 20 minutes before the onset of the bronchospasm reduces the likelihood of the thiopentone or the suxamethonium being the causative agent. Atracurium was administered intermittently with no obvious increase in the bronchospasm after any of the increments. The stability of the heart rate and blood pressure could have been due to the pre-operative use of pindolol. The only part of the management that apparently produced any permanent improvement in the bronchospasm was the substitution of the red rubber tracheal tube. Before tracheal intubation, this tube had been lubricated with lignocaine gel and this may have delayed direct contact between the rubber and the tracheal mucosa. Watkins[1] suggested the possibility of contact allergy response to red rubber tracheal tubes; this case may have been just such a reaction.

Pinderfields General Hospital, H.M. Basavaraja
Aberford Road, Wakefield, S. Firn
West Yorkshire WF1 4DG, J. Watkins
Supraregional Protein Reference Laboratory,
Royal Hallamshire Hospital,
Sheffield S10 2JF

Reference

1. Watkins J. Adverse anaesthetic reactions. An update from a proposed national reporting and advisory service. *Anaesthesia* 1985; 40: 797–800.

Cross-reactions of neuromuscular blocking drugs and anaphylactoid reactions

In their recent letter (*Anaesthesia* 1985; 40: 813–4) Watkins and Nimmo resolutely maintain the view that skin testing with neuromuscular blocking drugs is of doubtful value, that positive skin reactions to these drugs can be expected only in patients who have had previous exposure and that cross-reactivity to the drugs remains unproven.

In a detailed immunochemical study based on the clinical work initiated by Fisher over a decade ago,[1,2] we have unequivocally established the presence of reactive IgE antibodies in the sera of some patients who experienced anaphylactoid reactions to these drugs. The molecular basis of IgE antibody binding of six relaxants, alcuronium, tubocurarine, gallamine, suxamethonium, decamethonium and pancuronium, proved to be due to quaternary or tertiary ammonium ions present on all six drugs.[3–9] Immunological cross-reactivity was established by quantitative inhibition studies and inhibitory potencies in the nanomolar range left no doubt that the IgE antibodies were reacting with structurally similar determinants on the six different drugs. We would be most interested to learn if the views expressed by Watkins and Nimmo were formed with full knowledge of our immunochemical results and interpretations. If they were, we would welcome the chance to consider an alternative explanation(s).

Watkins and Nimmo suggest that skin testing, both intradermal and prick testing, should be carried out only when clinical and laboratory evidence strongly implicate an *immune* mediated reaction, not direct histamine release. However, they ignore the weight of evidence demonstrating the involvement and relationship between case histories, skin tests, presence of neuromuscular relaxant drug reactive IgE antibodies in the sera and clear-cut immunological cross-reactivities between the drugs. One wonders which laboratory tests and what sort of findings Watkins and Nimmo would accept as evidence strongly implicating an *immune* mediated reaction. In our studies, over 60 percent of patients who experienced an anaphylactoid reaction to alcuronium had alcuronium-reactive IgE antibodies in their sera. In the case of suxamethonium the figure was approximately 90 percent.[5–8]

The ostrich-like attitude to cross-reactivities of relaxants reflected in the letter of Watkins and Nimmo may also contribute to their belief that previous exposure to a relaxant is a necessary prerequisite for an immunologically-mediated anaphylactic reaction to a relaxant. Given the involvement of substituted ammonium ions as allergenic determinants of neuromuscular blocking drugs, and the widespread distribution of these determinants in our environment, the dogma of prior exposure should not always be readily accepted without question.

Watkins and Nimmo believe that the situation with regard to anaphylactoid deaths during anaesthsia is worsening. If this is so, it is not reassuring that investigators 'whose work on this particular topic is well established' can present recommendations based on an analysis that ignores a whole area of relevant research. This may, at best, be accepted as an oversight resulting in a lack of balance in the presentation of relevant scientific research findings; at worst, a view that ignores the existence of IgE-reactive cross-reacting allergenic determinants on relaxants could have dangerous consequences for some patients.

Kolling Institute of Medical Research, B.A. Baldo
Royal North Shore Hospital of Sydney,
St. Leonards, NSW 2065 and
Department of Medicine,
University of Sydney,
Sydney, Australia

References

1. Fisher MM. Severe histamine mediated reactions to intravenous drugs used in anaesthesia. *Anaesthesia and Intensive Care* 1975; 3: 180–97.

2. Fisher MM, Munro I. Life-threatening anaphylactoid reactions to muscle relaxants. *Anesthesia and Analgesia* 1983; **62:** 559–64.
3. Baldo BA, Fisher MM. Substituted ammonium ions as allergenic determinants in drug allergy. *Nature* 1983; **306:** 262–4.
4. Baldo BA, Fisher MM. Anaphylaxis to muscle relaxant drugs: cross-reactivity and molecular basis of binding of IgE antibodies detected by radioimmunoassay. *Molecular Immunology* 1983; **20:** 1393–400.
5. Baldo BA, Fisher MM. Detection of serum IgE antibodies that react with alcuronium and tubocurarine after life-threatening reactions to muscle-relaxant drugs. *Anaesthesia and Intensive Care* 1984; **11:** 194–7.
6. Harle DG, Baldo BA, Fisher MM. Detection of IgE antibodies to suxamethonium after anaphylactoid reactions during anaesthesia. *Lancet* 1984; **1:** 930–2.
7. Harle DG, Baldo BA, Fisher MM. Assays for, and cross-reactivities of, IgE antibodies to the muscle relaxants gallamine, decamethonium and succinylcholine (suxamethonium). *Journal of Immunological Methods* 1985; **78:** 293–305.

Neuroleptic-malignant syndrome

It was interesting to read the account of hyperpyrexia and muscle rigidity following overdose of imipramine in a patient also taking parstelin (*Anaesthesia* 1985; **40:** 1097–9) but surprising that Dr Peebles-Brown did not mention the neuroleptic-malignant syndrome (NMS), of which this case has several features.

A recent review[1] has defined the syndrome's diagnostic features of extrapyramidal symptoms such as catatonia and rigidity, together with autonomic dysfunction including tachycardia and hyperpyrexia. Szabadi cites recent work which suggests supersensitivity of dopaminergic receptors in the basal ganglia and hypothalamus as the cause of NMS. However, NMS may follow single doses of neuroleptic drugs and does not necessarily occur on re-administration.

Interestingly, no cases of NMS have been ascribed to tricyclic agents, but phenothiazines are commonly implicated (and the patient in question had taken parstelin which contains trifluperazine). Szabadi also points out the differences between NMS and malignant hyperpyrexia, in particular, that neuromuscular blockade is possible in NMS.

Anaesthetists working in intensive care may be called upon to provide supportive and therapeutic manoeuvres in cases of hyperpyrexia and should be aware of NMS, that drugs administered during anaesthesia may precipitate it and that it differs from malignant hyperpyrexia.

Department of Anaesthetics, J.W. Mackenzie
St Thomas's Hospital,
London, SE1

Reference

1. Szabadi E. Neuroleptic-malignant syndrome. *British Medical Journal* 1984; **288:** 1399–400.

A reply

Dr Mackenzie is quite correct to consider the inclusion of this case in the neuroleptic-malignant syndrome group, although, as he points out, it is not commonly associated with tricyclic compounds. Rigidity and hyperpyrexia are quoted in the data sheets for phenothiazines as possible side effects. This case nevertheless remains relatively unusual.

The most important aspect of reporting this case is, I agree, to bring the possibility of this reaction, and its differences from malignant hyperpyrexia, to the attention of other anaesthetists and intensive care workers, once again.

Basingstoke District Anne E. Peebles-Brown
Hospital,
Basingstoke,
Hants, RG24 9NA

Crystalloids are alive and well

In their review of peri-operative fluid administration, Dr Twigley and Dr Hillman (*Anaesthesia* 1985; **40:** 860–71) advocate the abandonment of certain current practices of crystalloid administration in patients undergoing surgery. Far from sounding the death knell of crystalloids, they give impetus to the ongoing crystalloid–colloid controversy, and throw their weight on the side of the colloid therapists. They go on to say that minor or moderate surgery patients do not need intravenous fluid infusion, if they are to drink within 24 hours, and suggest that it may be harmful.

In hypovolaemic patients, the question of the best resuscitation fluid is, as yet, unresolved. The diversity of regimens recommended in the literature suggests that there is no one ideal therapy and that several kinds of fluid can be used if vital signs, urine output and, when appropriate, filling pressures are monitored.[1] There are numerous studies to show that administration of crystalloids rarely causes problems of pulmonary oedema in the presence of a normal alveolar–capillary membrane.[2–4] In patients with leaky capillaries, colloids may leak across into the pulmonary oedema fluid, causing delayed resolution.[5] Colloids can also become trapped in 'third space' fluid, causing water-logging.[6,7]

In the presence of normal renal function, the kidney is the final determinant of fluid and electrolyte balance, provided a fluid providing balanced osmolar replacement, such as lactated ringers is administered.[6] Colloids can, however, be used effectively in the initial phase of management in a patient who is severely hypovolaemic and hypotensive to restore circulating blood volume quickly. Most surgical patients, especially with hypovolaemia, can tolerate electrolyte solutions because they can maintain an adequate colloid–hydrostatic gradient (colloid osmotic pressure–pulmonary artery diastolic or wedge pressure).[4]

In the absence of conclusive proof about the superiority of one regimen over another in respect of pulmonary function, crystalloids appear to have theoretical and practical advantages: extra buffering capacity and improved renal protection. Nevertheless, in an emergency, the most important consideration is rapid administration of adequate amounts, using whichever is readily available.[8] Crystalloids are easier to administer, are free from reactions and cost 5–10 percent of the cost of colloids.[9]

Ideally, all minor or intermediate surgical patients should have intravenous fluid therapy commenced prior to induction as a reliable vehicle for anaesthetic drugs, to counteract exaggerated pharmacological or adverse effects of any drug used during anaesthesia and to restore accumulated deficits.

Replenishment of fluid deficits protects the patient's homeostatic ability to compensate during induction and maintenance of anaesthesia. Surgery and anaesthesia are stresses and the patient should not be further challenged by the denial of intra-operative fluids. Furthermore, should any adverse reaction occur, for example anaphylaxis, the fluid-replenished patient is more protected and will be self-evidently easier to resuscitate with an intravenous infusion in place.

Department of Anesthesiology, R.A. Cajee
Children's Orthopedic Hospital and E.B. Furman
Medical Center,
and the University of Washington,
Seattle, WA 98105, USA.

References

1. Dodge C, Glass DD. Crystalloid and colloid therapy. *Seminars in Anesthesia* 1982; **1:** 293–301.
2. Rackow EC, Falk JL, Fein A, Siegel J, Packman M, Haupt M, Kaufman B, Putman D. Fluid resuscitation in circulatory shock: A comparison of the cardiorespiratory effects of albumen, betastarch, and saline solutions in patients with hypovolemic and septic shock. *Critical Care Medicine* 1983; **11:** 839–50.
3. Shires GT III, Peitzman AB, Albert SA, Illner II, Silane MF, Perry MO, Shires GT. Response of extravascular lung water to intra-operative fluids. *Annals of Surgery* 1983; **197:** 515–9.
4. Weil MH, Rackow EC. A guide to volume repletions. *Emergency Medicine* 1984; **8:** 101–10.
5. Lucas CE, Ledgerwood AM, Higgins RF, Weaver DW. Impaired pulmonary function after albumen resuscitation from shock. *Journal of Trauma* 1980; **20:** 446–551.
6. Furman EB. Blood and fluid replacement for paediatric patients. In: Steward DJ, ed. *Some aspects of paediatric anaesthesia.* Amsterdam: Elsevier/North-Holland Biomedical Press 1982; 79–100.
7. Furman EB. Massive transfusion in children. *Seminars in Anesthesia* 1984; **3:** 127–31.
8. Bristow A, Giesecke AH. Fluid therapy of trauma. *Seminars in Anesthesia* 1985; **4:** 124–33.
9. Ross A, Angaran D. Colloids vs. crystalloids—a continuing controversy. *Drug Intelligence and Clinical Pharmacy* 1984; **18:** 202–12.

A reply

Thank you for the opportunity to reply to the letter from Dr Cajee and Dr Furman. The answer to some of the specific questions in their letter gives me the opportunity to challenge some of the myths that are perpetuated in the continuing colloid–crystalloid debate.

There are some studies which compare the use of colloids and crystalloids and do not demonstrate any difference between them, but the results often reflect the shortcomings of current techniques used to measure the more subtle forms of peripheral and pulmonary oedema. Unfortunately, the authors of this letter have chosen as a reference to support the contention that crystalloids do not cause pulmonary oedema,[1] an excellent study which demonstrates the opposite. The group of patients resuscitated with isotonic saline in that study had an 87·5 percent incidence of pulmonary oedema, while the group resuscitated with colloid had a 22 percent incidence. Furthermore, it was a heterogenous group of patients, including those with sepsis, who presumably would have had 'leaky capillaries'. This, and other similar studies, which compare crystalloids with colloids in patients with 'leaky capillaries', indicate that colloid decreases rather than increases pulmonary and peripheral oedema.[2,3]

The suggestion that the kidneys are the 'final determinant of fluid and electrolyte balance' is largely why we have been able to get away with such a great variety of peri-operative fluid regimens for so long. Even the most severe fluid insults are tolerated as a result of compensation by the kidneys. It is this mechanism that enables us to 'tolerate electrolyte solutions', and not the fact that the crystalloids maintain an adequate colloid osmotic pressure (COP)–pulmonary artery wedge pressure (PAWP) gradient. In fact, the opposite is true. Crystalloid solutions reduce the COP and are a very inefficient way of increasing PAWP, because they are mainly distributed to the interstitial space, not the intravascular space. Interstitial fluid pressure rather than PAWP would be a better end point against which to titrate crystalloids.

It is necessary to have intravenous access even in minor surgery, but it may not always be essential to give intravenous fluids. The 'accumulated deficits' in minor surgery are minimal. If hypovolaemia, as measured by blood pressure, pulse rate and central venous pressure, occurs perioperatively, then it is more efficiently restored with fewer complications, by the use of a solution which is mainly distributed to that particular space, that is a colloid.[4] If adverse reactions, such as anaphylactoid shock occur, then adrenaline and colloid should be used rather than crystalloid fluid, most of which would not be mobilised from the interstitial space under such conditions.

Crystalloid solutions have no theoretical or practical advantages in respect of pulmonary function, in fact quite the opposite.[5] The buffering capacity of crystalloids is an abused term. It infers that an expanded interstitial space acts as a reservoir for a sudden depletion in intravascular volume. The reserve would be more efficiently kept on the shelf in the form of colloid, rather than in the interstitial space, where it causes peripheral and pulmonary oedema. The so-called renal protection offered by crystalloids is also misleading. The kidney is best protected by renal blood flow, which depends on the intravascular space, not the interstitial space. The fact that crystalloids are cheaper than colloids is also to be challenged. They are inefficient in restoring intravascular volume and therefore at least three times and up to ten times the amount has to be used. The cost of the increased morbidity from the complications of crystalloid would also have to be considered. Crystalloids are no easier to give than colloids. Both involve a cannula, giving set and a flask at the given height above the patient's heart. The reactions to colloid are extremely rare.[6] In an emergency, the most important consideration is to correct the hypovolaemia rapidly with the most efficient fluid (colloid), rather than using whatever is readily available, which would largely depend on the supplies officer, rather than the attending physician.

Crystalloids are only 'alive and well' in those patients where there is a proven and clinically significant depletion of the interstitial space, not simply as a mindless peri-operative ritual.

The Intensive Care Unit,
The Liverpool Hospital,
Liverpool, NSW, 2170,
Australia

K.M. HILLMAN

References

1. RACKOW EC, FALK JL, FEIN IA, SIEGEL JS, PACKMAN MI, HAUPT MT, KAUFMAN BS, PUTNAM D. Fluid resuscitation in circulatory shock: a comparison of the cardiorespiratory effects of albumin, hetastarch, and saline solutions in patients with hypovolemic and septic shock. *Critical Care Medicine* 1983; **11:** 839–50.
2. OTTOSSON J, DAWIDSON I, BRANDBERG A, ERIKSSON B. Experimental septic shock: relative effects of treatment with antibiotics, crystalloid or colloid solution infusions and corticosteroids. *Critical Care Medicine* 1985; **12:** 560–4.
3. KAUFMAN BS, RACKOW EC, FALK JL. The relationship between oxygen delivery and consumption during fluid resuscitation of hypovolemic and septic shock. *Chest* 1984; **85:** 336–40.
4. HILLMAN KM. Fluid and electrolyte management in the critically ill. *Archives of Emergency Medicine* 1984; **1:** 9–15.
5. TWIGLEY AJ, HILLMAN KM. The end of the crystalloid era? A new approach to peri-operative fluid administration. *Anaesthesia* 1985; **40:** 860–71.
6. RING J, MESSMER K. Incidence and severity of anaphylactoid reactions to colloid volume substitutes. *Lancet* 1977; **1:** 466–9.

Epidural analgesia in the presence of fever

The letter from Dr Behl about epidural analgesia in the presence of a fever (*Anaesthesia* 1985; **40:** 1240–1) raised some interesting questions. A similar problem occurred to me recently when a 24-year-old primigravida, 39 weeks gestation was admitted in established labour after an uncomplicated pregnancy. On admission she was apyrexial, normotensive and having regular painful contractions. The fetal heart rate was 140 beats/minute with normal beat-to-beat variation.

Lumbar epidural analgesia was established soon after admission and labour continued for a further 6 hours until the patient developed a sustained pyrexia of 39°C, though no focus of infection could be found. The site of insertion of the epidural catheter had become erythematous, but this was probably not significant; however, the catheter was removed and analgesia continued with Entonox and intramuscular pethidine. An hour later, the fetus developed a persistent tachycardia of between 180 and 220 beats/minute and a Caesarean section was undertaken under general anaesthesia.

Direct laryngoscopy unexpectedly revealed gross oedema of the larynx and the posterior pharynx, which made tracheal intubation very difficult though not impossible. Anaesthesia and surgery were subsequently uneventful, though postoperatively, the patient developed a sore throat and tender lymphadenopathy of neck nodes, of viral origin, which resolved within a week.

The question raised from this particular case was should the epidural cathether have been removed? We not only denied the patient adequate analgesia for the last few hours of labour, but subjected her to the risks of a general anaesthetic, compounded by the presence of laryngeal and pharyngeal oedema, the most likely cause of the pyrexia.

The Royal Marsden Hospital,
Fulham,
London, SW3 6JJ

D.G. THOMAS

Priming volume of epidural equipment

There continues to be a controversy about the exact dose of local anaesthetic and of adrenaline which should be administered as an epidural test dose.

It is obviously the volume of fluid discharged from the end of the catheter which matters, rather than the volume which leaves the syringe. The difference, which is the priming volume of the filter and catheter, tends to be forgotten, even though it can represent a substantial proportion of the test dose.

The volume of saline required to prime 14 Portex epidural catheters and the attached filter was measured. Seven were fitted with Millex OR filters and seven with Portex flat filters. The volume required varied from 0.7–0.8 ml, with the Millex filters, and from 1.0–1.1 ml with the Portex filters.

Either the filter and catheter should be filled with the solution used for the test dose before insertion (thus also confirming the patency of the catheter) or the size of the test dose should be adjusted to compensate for the losses involved in priming. It would also be helpful if the manufacturers indicated the dead space of their products on the packaging.

Department of Anaesthesia,
The Royal Victoria Infirmary,
Newcastle upon Tyne,
NE1 4LP

J. OYSTON

Bradycardia and hypotension in spinal anaesthesia

R.J. Purnell reported (*Anaesthesia* 1985; **40:** 1245) a case of bradycardia and hypotension associated with spinal anaesthesia in a patient undergoing a transurethral resection of prostate. He attributed this event to the fact that the patient was receiving verapamil and that the hypotension was aggravated, he postulated, by a dilutional hypocalcaemia as a result of the absorption of irrigation fluid.

May I suggest that the bradycardia and hypotension were due to cardiac sympathoplegia. The author recorded that 2 ml heavy cinchocaine was used and that the level of block extended to T_{10}. However, the block may well have extended higher than this as time progressed and is especially likely if a slight head-down tilt is employed, though this was not recorded in this case.

Cardiac sympathetic fibres are Group B fibres and are exceedingly sensitive to local anaesthetics, so that sympathetic blockade may extend higher than the level suggested by loss of somatic sensation.

Belfast City Hospital,
Belfast, BT9 7AB

C. MCLOUGHLIN

Generalised oedema and epidural analgesia

The report of Dr Kirby and Dr Ryan (*Anaesthesia* 1985; **40:** 709–10) on this subject raises practical points. In the presence of marked lumbosacral oedema, the oedema fluid causes dilution of the bupivacaine to a negligible concentration. The characteristics of the oedema fluid may be important and a protein rich oedema fluid, such as the authors found, might further remove bupivacaine by protein binding. Finally, the bupivacaine pKa may be altered in an oedematous area.

This, at least, has been the clinical experience in this centre in grossly oedematous patients, as described by the authors. Intradural analgesia has been successful in these, though not as a continuous technique. Perhaps the leakage of fluid described was a mixture of cerebrospinal and oedema fluid and their patient did not get a headache because the excess extracellular fluid helped maintain the intradural hydrostatic pressure at a level high enough to avoid symptoms developing.

Department of Anaesthesia,
Rotunda Hospital,
Dublin 1

J. GARDINER

Stability of diamorphine–sodium chloride solutions

The letter from Dr Hain and Dr Kirk (*Anaesthesia* 1985; **40:** 1241) about the solubility of diamorphine hydrochloride in 0.9 percent sodium chloride under the heading 'stability of diamorphine–sodium chloride solutions' was interesting. They appear to have been using a solution of 0.5 mg/ml in sodium chloride

0.9 percent for parenteral infusion. We commonly use a similar solution, prepared immediately before administration, for epidural analgesia. Martindale[1] warns that sodium chloride may precipitate diamorphine from *concentrated* solutions; by no stretch of the imagination could this stricture apply to 0.5 mg/ml or 0.05 percent. The experiment Dr Hain and Dr Kirk have carried out employed a solution 100 times this concentration.

Please let it be made clear to your readers that concern about *solubility* of diamorphine is a complete red herring. *Stability* is the important factor. Surely it is well known that diamorphine hydrochloride in aqueous solution degrades spontaneously at room temperature to both 3- and 6-monoacetylmorphine and thence to morphine.[1] Why else would it be supplied as a powder in ampoules? By preparing it for slow infusion over many hours, your correspondents have hit upon a rather novel way of administering morphine to their patients! (Cost of diamorphine 5 × 10 mg ampoules: £3.36; cost of morphine 5 × 10 mg ampoules: £1.13.)

The action of diamorphine is dependent upon its metabolites, at least in part, if not entirely. It should be understood, therefore, that diamorphine is not more potent than morphine, as stated in the Extra Pharmacopoeia; rather, it is simply a lipid-soluble and therefore quick-acting version of morphine. It is thus capable of eliciting a kick when main-lined, unlike morphine, and thereby hangs its abuse-potential. Because of its more ready access to the site of action, the effect of diamorphine may be more profound initially. There can be little value in giving diamorphine rather than morphine by continuous infusion, even were this feasible, since speed of onset is largely irrelevant to such a mode of administration.

Anaesthetic Unit, FELICITY REYNOLDS
St Thomas's Hospital Medical School (UMDS)
London, SE1 7EH

Reference

1. MARTINDALE. *The Extra Pharmacopoeia*, 28th edn, London: The Pharmaceutical Press, 1982, p. 1008.

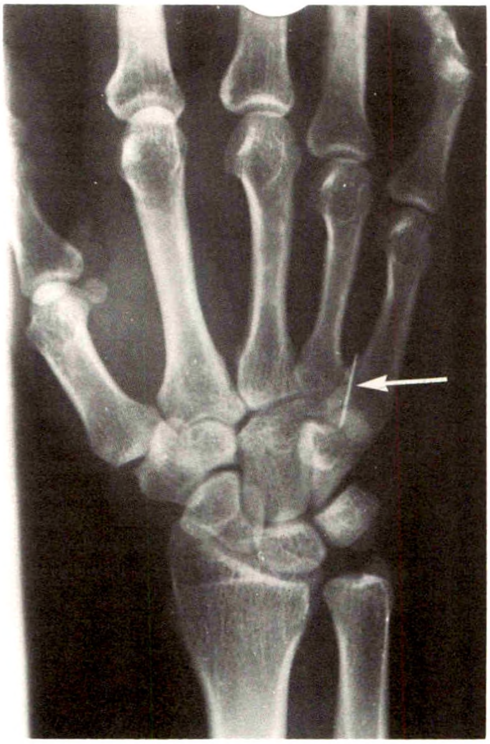
An unusual complication using a Butterfly needle

Winged needles are commonly used for venous access during anaesthesia. Complications of their use are normally confined to loss of this venous access, either by blockage of the needle, or by the needle 'cutting out' of the vein. (In the latter case the possibility of tissue damage due to accidental subcutaneous injection of drugs can be a real problem.[1]) The incidence of these complications varies from 15 percent reported by Sale[2] and 16 percent reported by Harvey[3] up to 39 percent reported by Duffey and Lee.[4]

This is a report of the case of a thirty-eight-year-old patient who underwent surgery for routine haemorrhoidectomy. Venous access was established using a 23-SWG Abbott Butterfly placed in a vein on the dorsum of the hand. Anaesthesia was then induced with 500 mg thiopentone and maintained with 33 percent oxygen in nitrous oxide, supplemented with halothane breathed spontaneously from a facemask and Mapelson A system. The operation lasted approximately 30 minutes and was uneventful; during this time, no further intravenous drugs were given.

Initially in the recovery room the patient was restless. However, once he had become settled and had regained consciousness the Butterfly was removed. Examination of this indicated a large part of the metal needle was missing; an X ray of the hand (Fig. 1) showed this missing portion to be located close to the site of skin puncture (arrowed).

The needle was subsequently removed under a second general anaesthetic without any further problems. In view of this case, perhaps examination of Butterflies removed in recovery wards should be more stringent than at present.



Department of Anaesthetics, A.P. WHITE
St Mary's Hospital,
London W2

References

1. Green R. The Butterfly needle. *The Medical Protection Society Annual* 1981; 20.
2. Sale JP. The use of 'butterflies'. *Anaesthesia* 1984; **39:** 294.
3. Harvey D.C. Reliability of 'Butterfly' needles during anaesthesia. *Anaesthesia* 1983; **38:** 1102.
4. Duffy BL, Lee JS. Intravenous access: a comparison of two methods. *Anaesthesia and Intensive Care* 1983; **11:** 135–7.

A reply

Thank you for the opportunity of responding to Dr White's case report of an incident with a 23G Butterfly needle which was, unfortunately, not returned to the Company for technical appraisal.

A similar case was reported to us over 10 years ago; the metal shaft of a Butterfly needle fractured as a result of restless movements of the hand during the immediate postoperative period in an elderly patient. This misfortune must occur extremely rarely, despite the widespread use of this type of needle during, and immediately after, operations. We agree that examination of winged steel cannulae after removal ought to be routine for doctors and nurses in a similar manner to that used customarily, for example, on withdrawal of epidural catheters. Existing experience does not, however, indicate that this a frequent problem.

Medical Adviser,
Abbott Laboratory,
Queenborough,
Kent, ME11 5EL

F.E. Bennetts

Pain in the orbit: a feature of dural tap

Spinal headache is a recognised feature in the first 3 days after dural tap. It is often occipital, but may be vertical or frontal and pain may spread to the shoulder or in the distribution of cervical nerves.[1] Headache is initiated or made worse by adoption of sitting or erect posture. Often neck stiffness may be present. A case is described where pain in the orbit occurred after dural tap.

A thirty-year-old, fit multigravida requested an epidural for pain relief during labour. She had no history of headache or migraine and she received no medication other than iron. She had had two epidurals in the past for pain relief during labour. On this occasion, the epidural was started in the left lateral position in the L_{3-4} interspace. The epidural space was encountered with difficulty and only after a few attempts, but the catheter could not be threaded and the catheter and Tuohy needle were removed. There was no sign of dural tap. Epidural puncture was successful at the L_{2-3} interspace and the catheter was passed. Again, there was no sign of dural tap. A test dose of 0.5 percent bupivacaine 2 ml, was followed by a dose of 6 ml 0.5 percent bupivacaine for analgesia. The patient complained of severe pain in the left orbit. The level of block extended from T_{10} to L_3 after 20 minutes. Hypotension responded to fluid infusion, but the patient was nauseated and vomited. Paracetamol was given for headache, which was relieved after a few hours. She required three incremental doses of bupivacaine, but there was no change in the extent of the block. The catheter was removed after delivery. Twenty-four hours later, the patient complained of a characteristic (spinal) headache with neck stiffness. She was treated conservatively at first with fluid infusion, rest and analgesics but this failed to relieve the headache. An epidural blood patch was done the next day and the headache was relieved within hours.

The causation of the headache is debatable,[2] but the majority view favours low cerebrospinal fluid pressure from leakage from the dural puncture site. This results in changes in the haemodynamics of cerebrospinal fluid and loss of cushioning of the brain with pressure, and traction on the vessels and sensitive structures of the brain such as the basal dura and tentorium.[3] The pain occurred within 15 minutes of the epidural, so a change in haemodynamics is suspected. Dural tap was not obvious at the time, but subsequent clinical features suggested dural tap and, in fact, the diagnostic epidural blood patch did cure the headache. This procedure has been suggested in cases of unrecognised dural tap.[4]

It is concluded that pain in the orbit may be a presenting feature of dural tap and we have experience of one other patient who had an obvious dural tap who also complained of pain in the orbit within half an hour of the incident.

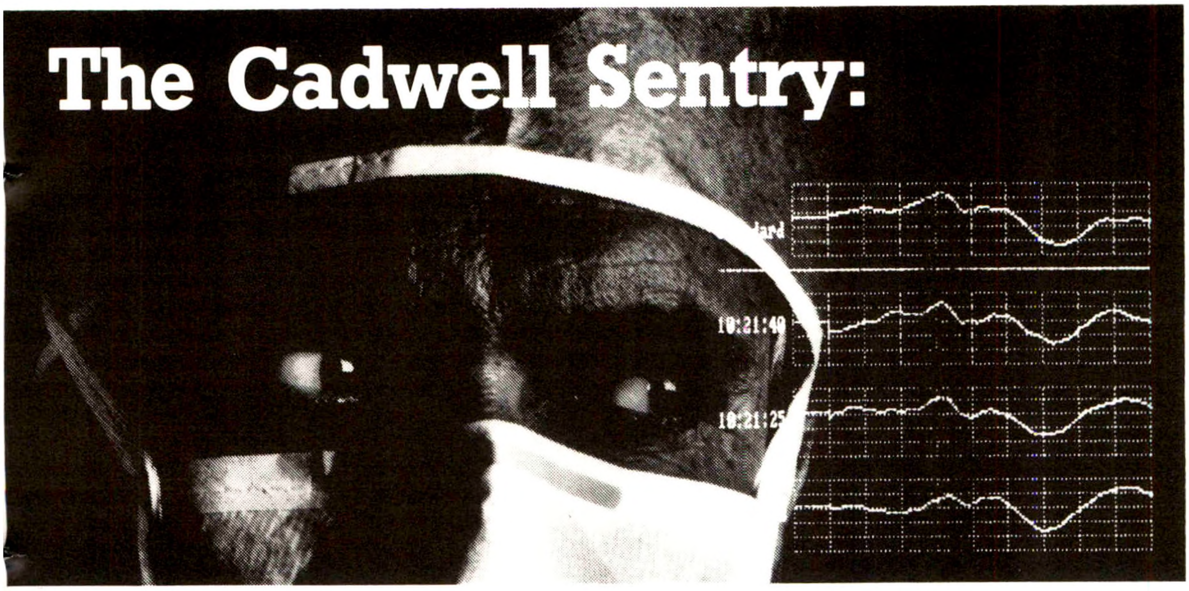
South Cleveland Hospital,
Middlesbrough,
Cleveland

C.M. Kumar
B. Dennison

References

1. Atkinson RS, Rushman GB, Lee JA. *Synopsis of anaesthesia*, 9th edn. Bristol: Wright, 1982, 748.
2. Bonica JJ. *In: Obstetrical anesthesia: current concepts and practice.* Schnider SM, Melbourne: Krieger, 1973, 174.
3. Atkinson RS, Rushman GB, Lee JA. Synopsis of Anaesthesia, 9th edn. Bristol: Wright 1982, 750.
4. Shah JL, Veness AM. Epidural blood patch using a catheter. Diagnosis of an unrecognised dural tap. *Anaesthesia* 1985; **40:** 1120–3.

The Cadwell Sentry:



Faster updates . . . greater protection

The Cadwell Sentry: a powerful new advance in monitoring evoked potentials during neuro-surgical cases. The only evoked potential monitor that gives you 15-second updates of ongoing neurologic activity.

PUSH ONE BUTTON . . .

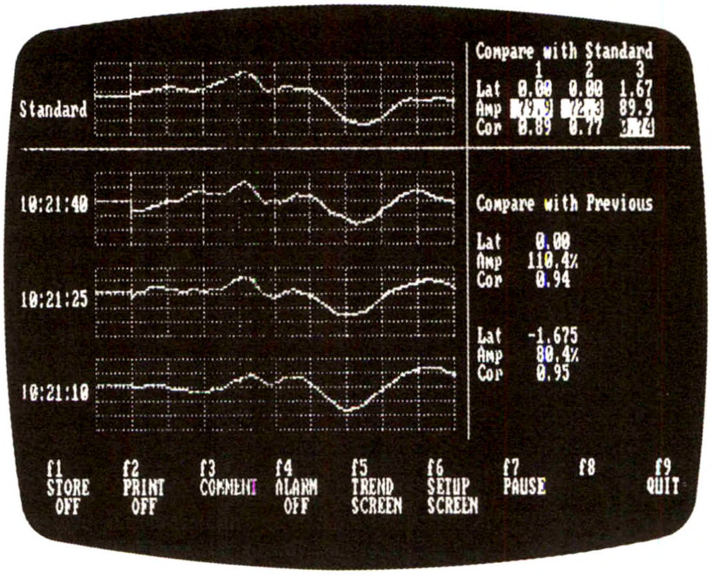
The Cadwell Sentry immediately directs your Cadwell evoked potential instrument, gathers, processes, and displays the averaged responses.

ONCE EVERY 15 SECONDS . . .

. . . And continuously measures each 15-second average for you, quickly alerting you to any critical changes in waveform components.

ALL AUTOMATICALLY.

ALL CONTINUOUSLY.

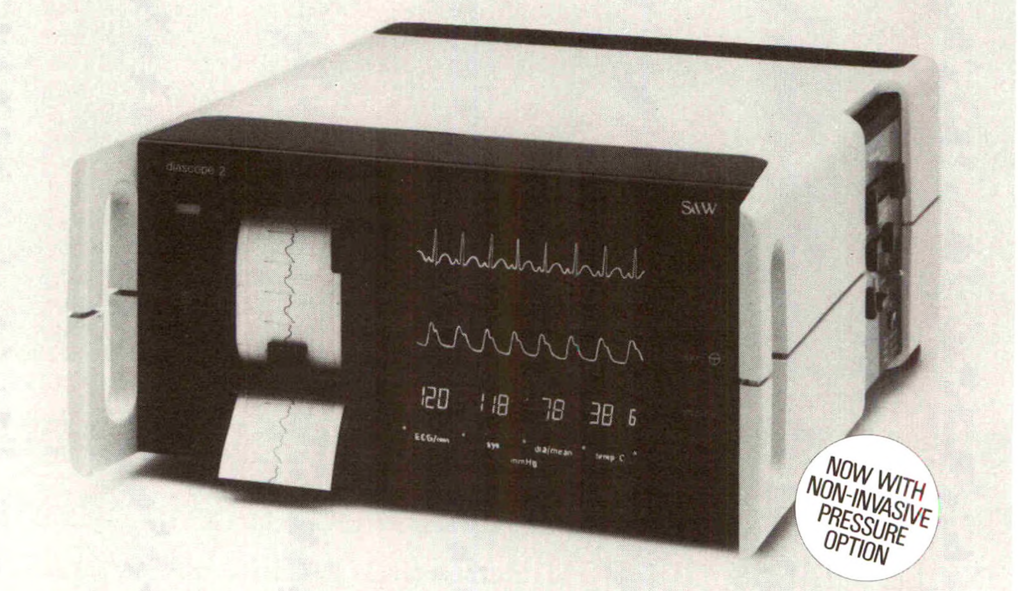


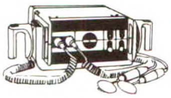
```
                    Compare with Standard
                          1     2     3
Standard            Lat  0.00  0.00  1.67
                    Amp  79.9  72.3  89.9
                    Cor  0.89  0.77  0.74

10:21:40            Compare with Previous

                    Lat    0.00
                    Amp  110.4%
                    Cor    0.94
10:21:25

                    Lat  -1.675
                    Amp   80.4%
                    Cor    0.95
10:21:10

f1     f2     f3       f4     f5      f6      f7     f8    f9
STORE  PRINT  COMMENT  ALARM  TREND   SETUP   PAUSE        QUIT
 OFF    OFF             OFF   SCREEN  SCREEN
```

WORLD HEADQUARTERS
Cadwell Laboratories, Inc., 1021 N. Kellogg Street, Kennewick, WA 99336
Telephone: Washington State 5097356481 Telex: 152514

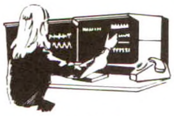
EUROPE AND MIDDLE EAST
Cadwell Europe Ltd, Still House, 29 East Street, Farnham, Surrey GU9 7SW
Telephone: (0252) 727007 Telex: 858623 & 858293

S&W

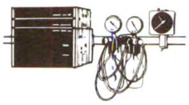




Defi 2
multipurpose defibrillator

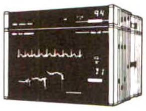


Central Station
up to 12 patients monitored and recorded.

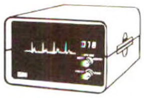


Modura Rail
The original "Danish Rail" system

Medicart
Multipurpose trolleys designed especially for medical use.



8000 series
– the complete flexible monitoring system



Diascope 1
single channel, compact ECG monitor

Simonsen & Weel ... care

Diascope 2 is a range of portable configured monitors. All models include integral ECG and temperature amplifiers, together with a twin channel display incorporating alpha-numeric indication of heart rate and temperature.
User specifiable parameter options include pressure (separate options for both invasive and non-invasive), peripheral pulse and respiration, while all units can be specified to include an integral chart recorder.
The wide variety of options available means that the Diascope 2 can be used throughout the hospital in A&E, the Operating Theatre, ITU/CCU, or Special Care Baby Units. A battery option which can be specified into all available models allows transport within, or to-and-from the hospital. Another truly versatile range of monitors – further proof that Simonsen and Weel care . . .

Simonsen & Weel Ltd. Ruxley Corner, Sidcup, Kent DA14 5BL Tel: 01-309 0433 Telex: 896328

Mask for child resuscitation

A recent report[1] emphasised the importance of training nurses in cardiopulmonary resuscitation and stated that those on the scene of arrest should start resuscitation with a bag and mask. The most common cause of cardiac arrest in children is respiratory in origin, so initial resuscitation with bag and mask is critical.

The Rendell-Baker Soucek mask[2] is regarded as a standard mask for paediatric anaesthesia, and it is often used as the mask for resuscitation. However, it is not always easy to obtain a good fit, especially when it is used by untrained personnel. There should be a mask which is easy to handle by everyone.

We examined the Rendell-Baker Soucek mask and the new Laerdal mask in use on a CPR mannequin, to test their efficiency in terms of ventilation of the lungs and degree of leakage. Thirty nurses without special training in resuscitation participated in the study. The nurse held the mask on the Resusci-Baby (Laerdal) and performed bag and mask ventilation with the Laerdal child resuscitator. The resuscitator stroke volume was measured between the resuscitator and the mask. The lung inflation volume was also measured at the end of the mouth-to-lung tube of the Resusci-Baby. The difference between the resuscitator stroke volume and lung inflation volume was called the leak. Student's paired *t*-test was utilised for statistical analysis.

	Resuscitator stroke volume Mean, ml (SD)	Lung inflation volume Mean, ml (SD)	Leak Mean, ml (SD)
Rendell-Baker Soucek mask	258 (30)	76 (63)	182 (58)
Laerdal mask	248 (46)	196 (46)	52 (50)
t-test	NS	$p<0.001$	$p<0{\cdot}001$

A much greater leak was recorded with the use of the Rendell-Baker Soucek mask. The Laerdal mask provided a better seal around the mouth and made inflation of the lungs easier. The Laerdal mask seems, at least in inexperienced hands, much more useful for resuscitation purposes than the Rendell-Baker Soucek mask.

Department of Anaesthesia,
Ibaraki Children's Hospital,
Mito, 311-41,
Japan.

M. Yamashita
K. Motokawa

References

1. Barcroft J. Resuscitation skills. *Anaesthesia* 1985; **40:** 1015–6.
2. Rendell-Baker L, Soucek DH. New paediatric face masks and anaesthetic equipment. *British Medical Journal* 1962; **1:** 1690–3.

An unusual epidural needle

This unusual Tuohy needle, which may be of interest to your readers, was found amongst some old anaesthetic equipment (Fig. 1). The needle is 16.2 cm long from tip to hub. However, its shaft is short, 7 cm from tip to wings. The needle has, at the hub, Mackintosh wings and Odom's indicator.[1] The latter is made of a glass capillary tube housed in a glass and metal cover. An air bubble in the capillary would be visibly sucked inwards when the tip of the needle enters the extradural space.

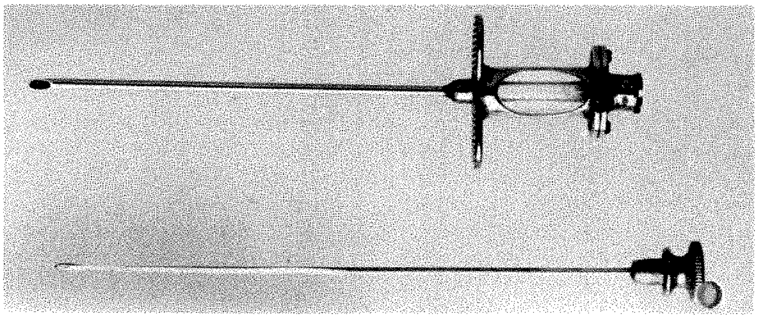
A search of the literature has not revealed the origin of such a needle with the combination of wings and indicator and the writer would be most interested to hear from any of your readers who have seen this needle before.

Department of Anaesthetics,
Selly Oak Hospital,
Birmingham, B29 6JD

S.M. Mostafa

Reference

1. Odom CB. Epidural anaesthesia. *American Journal of Surgery* 1936; **34:** 547.



Nosworthy anaesthetic record

Professor Norman's letter (*Anaesthesia* 1985; **40:** 1238–9) evokes a touch of nostalgia, for I too kept my first one hundred anaesthetics on Nosworthy cards. I also used to keep several hundred literature references on punched cards, and have worked in an anaesthetic department where all the anaesthetics (around 7000 a year) were recorded on an A4 size card. I can assure Professor Norman that when more than a few hundred cards are kept, the cards are no longer easy to use, store or classify, nor are they even cheap.

In the Städtischen Kliniken, Osnabrück, West Germany, the punched card anaesthetic record system has been replaced by a microcomputer program. The system, which has now been running for 3 years, has space for more than double the amount of information on the Nosworthy card, and yet can pack
records onto two floppy discs. A search of
year's records to produce a tabular classifi
patients' age and sex and by surgical speciality
to extract the numbers of cards on which a
feature, or combination of features, has bee
takes around 12 minutes.

I can supply those interested with deta
program, which runs on the Apple II series
computer.

Intensive Care Unit,
Derbyshire Royal Infirmary,
Derby

P.H.

Hazards with a Mediplast Coax 2 system

We have experienced a serious problem recently with the Coax 2 Bain system manufactured by Mediplast, Sweden. Splits in, and complete detachment of, the (red) fresh gas tube from the angled fixed connector have occurred on many occasions in recent months. These always occur around the line of glue between the two pieces of plastic, at a point where kinking may often occur if one is not careful.

The manufacturers tell us that this has not been previously reported. Contrary to their instructions, it is our practice to re-use this system, which is marketed for a single patient's use. The British suppliers' of the system tell us that this is common custom. However, we have noticed that this can occur after a single day's use.

The first sign of wear is a partial, circumferential split in the tubing, which may then rapidly progress to a full thickness split or even detachment. We therefore recommend that kinking should be avoided when this system is in use. The (red) fresh gas tube should not be pulled or stretched and the junction with the angled connector should be inspected before, during and after every use. The system must be discarded and replaced at the first sign of any fault. The manufacturers might consider that a short rubber, or spring reinforced, sleeve should be introduced at this junction to prevent the fresh gas tube from kinking.

Arrowe Park Hosptal,
Upton,
Wirral,
Merseyside, L49 5PE

J.E.

A reply

My firm is not the manufacturer of this prod
do distribute the Coax 1 and 2 systems thro
United Kingdom.

We have not had this complaint before an
it is difficult to visualise how cracking and
could occur. The red fresh gas tube is one c
length from distal to proximal end and is fir
into position.

The manufacturers do state that the Coax
for *single use* only, although, of course, we
that a number of anaesthetists do use them
than one occasion.

Cory Bros,
4, Dollis Park,
London, N3 1HG

G. C

An improved pressure infusor

Increased pressure is often applied to air above a fluid, to aid its rapid infusion, by means of a pressure infusor. This apparatus has several well recognised shortcomings. Inflation of the bladder with the standard bulb is cumbersome, time consuming and, if performed repetitively, exhausting. When the bag of fluid empties, either the head of pressure, and thus the flow rate, decreases or more time and effort is needed to pump up the bladder. The use of an automatic tourniq
to power the pressure infusor has alre
described.[1] Inflation is thus quicker and
physical exertion, and once the bladder is in
pressure remains constant with higher
infusion rates. However, unless the infusor
manually deflated, difficulty and delay may o
the fluid containers are changed. We ha

modified the apparatus to overcome this by attaching a suction outlet to the bladder, which thus allows active deflation.

In our modification of a one-litre Abbott pressure infusor (Fig. 1), the bulb is removed and replaced by a three-way tap. The pressure infusor bladder is connected via the tap to the output from a Stille automatic tourniquet and to suction. The pressure infusor tap is opened to the automatic tourniquet box to inflate. The tap is turned 90° to connect the pressure infusor to the suction to deflate.

This system works well in clinical practice and the advantages are demonstrated in Table 1. In summary, physical effort is not needed, less attention is required to work the apparatus, thus leaving more time for the patient, fluid is infused faster and active deflation using suction considerably shortens bag change-over times.

Broomfield Hospital,
Chelmsford,
Essex CM1 5ET

D.R. Goldhill
T.J. Dines
A.J. Clark

Reference

1. White AP. A powered pressure infusor. *Anaesthesia* 1984; **39:** 729.

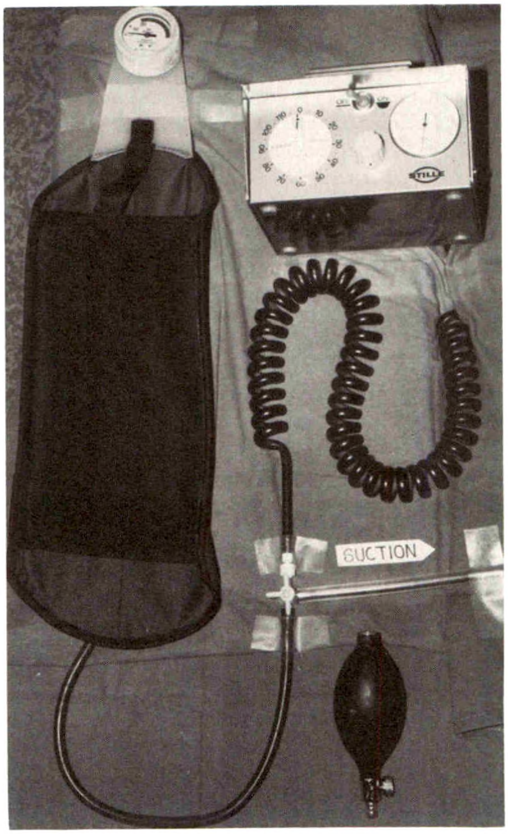


Table 1.

Times	Standard one litre pressure infusor	Modified apparatus	
Inflation (seconds)*	26.4	19.4	
Infusion (seconds)†	223.4	172.8	
		Without suction	With suction
Deflation (seconds)‡	46.1	20.8	5.0
Bag change (seconds)§	70.1	38.7	27.8

*Inflation time to 300 mmHg pressure.
†Time to infuse 500 ml of 0.9 percent NaCl pressurised to 300 mmHg through 18-G Venflon cannula.
‡Deflation time from pressure of 300 mmHg until 1 Kg weight pulls empty fluid bag from pressure infusor.
§Time to remove empty bag at 300 mmHg pressure, extract administration set, re-insert set into full bag and repressurise.
The order of measurements was randomised. Results are average of five readings.

Multiple cannulation of a single vein

We read Dr Turtles' letter (*Anaesthesia* 1985; **40:** 1243) with interest. It is not clear, however, from the description whether a theoretical technique or his actual clinical practice has been described. Unless vein dilators are used, large bore cannulae cannot be fed over ordinary guide wires because of the disparity in size. If vein dilators *are* used, then an extremely large bore cannula can be inserted over a small wire. Further guide wires could be inserted through the cannula for the purpose of establishing more than one central venous infusion. This would not be reasonable in practice. Firstly, it would be expensive and, secondly, it would leave several small catheters traversing a large hole in the vein.

It is far simpler to introduce a double- or triple-lumen catheter, using a single guide wire. These catheters are not widely used in this country, because of their high cost. We have used a double-guide wire technique in the internal jugular vein without complication in over 100 patients for cardiac surgery. The first guide wire is introduced into the vein via a 1.1 mm (19-G) metal needle (Vygon Leader Cath 115.12). The wire is left in place and the needle removed. A second needle is then introduced into the vein, cephalad to the first wire, and the second wire inserted. The two catheters are introduced over the wires and firmly secured. The first catheter is not threaded over the wire at first, to avoid the risk of hitting it with the second needle. It is theoretically possible that the wire might be hit with the second needle, but this has never happened in clinical practice.

If the continuing morbidity and mortality associated with central venous catheterisation is to be minimised, the use of rigid cannulae over long needle devices should be phased out. These devices are particularly dangerous in the hands of the inexperienced clinician and when the vein is difficult to locate. Seldinger techniques are preferable. The suggestion that long cannulae with trocars should be inserted to their full extent before removing the trocar[1] is a recipe for mortality.

Department of Anaesthetics,
University Hospital of Wales,
Cardiff, CF4 4XW

I.P. LATTO
P.J. HILTON

Reference

1. WITHINGTON PS, CARTER JA. Hazards in multiple cannulation of a single vein. *Anaesthesia* 1985; **40:** 700.

External jugular vein catheterisation

Catheterisation of the external jugular vein is particularly useful when no other peripheral vein is left for infusion and a central venous catheter is either useless or not required. The technique as well as the difficulties of this venepuncture are well known. One of the problems faced is that the jaw is often in the very place where either the syringe or the operator's hand needs to be in order to position the needle at the appropriate angle to the skin. This problem is often found in adult patients and is even more acute in neonates and infants. It may result in multiple skin punctures and, eventually, in failure to catheterise the vein.

There is a very simple solution to this problem: one just has to bend the needle gently as shown in Fig. 1, so that the operator's hand can reach just over the mandible bone and allow proper venepuncture. This method has been used for over 100 patients, mainly premature neonates and infants, and was found to be fully satisfactory, even by operators who very seldom use the external jugular vein.

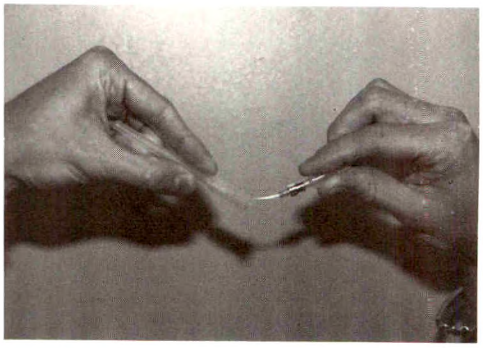


Fig. 1.

Departément d'Anesthesie—
Reanimation,
Centre Hospitalier General,
Robert Ballanger,
93602 Aulnay-sous-bois, France

P. BOUJU
H. DREUX-BOUCARD
J.-F. AMIOT
J.H. PALACCI

A simple aid to central vein cannulation

A syringe with a spring-loaded plunger (Pallin, one hand aspirating syringe; Steriseal) can be helpful in confirmation of central vein venepucture. An aspirating syringe of this type may be attached to the hub of a cannula-over-needle or Seldinger-type needle. The spring is kept compressed until the point of the attached needle has been inserted through the patient's skin. The syringe can then be released, allowing the operator to devote his full attention to directing the needle; venepuncture is confirmed by a flashback of blood.

Department of Anaesthetics,
Raigmore Hospital,
Inverness IV2 3UJ

A. MACNEIL

Another aid for the insertion of nasogastric tubes

The letter from Dr Conacher (*Anaesthesia* 1985; **40:** 1246–7) was interesting and prompts me to suggest another aid to the insertion of a nasogastric tube into patients with tracheal tubes in place and in whom the insertion of a nasogastric tube is difficult. My technique is similar to that of Dr Conacher.

Most nasogastric tubes have side holes. The selected tube is passed through the nostril and its end is taken out through the mouth either manually or with the help of forceps. One metre of strong suture material (for example, Ligapak Linen Ethicon 135) is threaded through the eye of a half-circle strong needle (Steriseal Mayo's trocar 35 mm No. 4) and passed through the distal two holes of the nasogastric tube. The two ends of the suture material are passed through 1 cm proximal to the distal end of the well lubricated large bore stomach tube (for example, Ch34 LeyMed, red rubber) with the needle. The two ends of the suture are pulled together to approximately the two tubes which are then advanced from the mouth into the oesophagus and stomach. The two ends of the suture are held firmly and, when the position of the nasogastric tube has been confirmed, one end is released and pulled out. The stomach tube is then removed. This technique has been useful for difficult cases in whom the insertion of the nasogastric tube has been achieved without trauma.

South Cleveland Hospital,
Marton Road, Middlesbrough,
Cleveland

C.M. Kumar

Evaluation of Ivac 560 volumetric pump

Drs Hutchinson, Yeoman and Byrne (*Anaesthesia* 1985; **40:** 996–9) report on an evaluation of the Ivac 560 volumetric pump. The continuing evaluation programme sponsored by the UK Health Departments also features infusion instruments and the Ivac 560 is evaluated in *Health Equipment Information* (HEI) No. 147, October 1985. The DHSS, programme is essentially one of comparative evaluation in the form of a best buy guide and your readers may be interested to compare the format and findings of the HEI evaluation with the Hutchinson paper. For example, some 10 points of non-compliance with BS 5724 Pt 1 were found on the DHSS model tested.

The *Anaesthesia* article refers to HEI No. 96 of September 1981. This is perhaps not the most appropriate issue, since it was mainly concerned with drip rate pumps and controllers, whereas the Ivac 560 is a volumetric pump HEI 96, 106, 116, 125, 135 and 147 have been devoted to infusion pumps.

The DHSS is attempting to make HEI more widely used in NHS purchasing and comments on the publication to the editor are always welcome. Forthcoming evaluations are announced in each issue; further information is available on request.

Department of Health
and Social Security,
Scientific and Technical Branch,
14 Russell Square,
London WC1B 5EP

D.B. Revell

Anaesthesia, 1986, Volume 41, pages 562–567

Book reviews

Current Topics in Anaesthesia. Management of Postoperative Pain 562
MARGARET E. DODSON
Anaesthesia for Eye, Ear, Nose and Throat Surgery 563
J.D. MORRISON, R.K. MIRAKHUR AND H.J.L. CRAIG
Anesthesia for ambulatory surgery 563
Edited by B.V. WETCHLER
Cardiac Arrhythmias (Practical Notes on Interpretation and Treatment) 564
D.H. BENNETT
Anaesthetic Equipment 564
C.S. WARD
Understanding Anaesthesia Equipment. Construction, Care and Complication (2nd edition) 565
J.A. DORSCH AND SUSAN E. DORSCH
Monitoring in Anaesthesia and Critical Care Medicine 565
Edited by C.D. BLITT
1985 Yearbook of Anaesthesia 566
R.D. MILLER, R.R. KIRBY, G.O. OSTHEIMER, L.J. SAIDMAN AND R.K. STOELTING
A Doctor in Saudi Arabia 566
G.E. MOLONEY

Brief Reviews of books received by the Editor
Health Equipment Information No. 153: Evalua- of Resuscitators 567
Capnography in the operation room: an introductory directory 567

Current Topics in Anaesthesia. Management of Postoperative Pain

MARGARET E. DODSON. Pp. 274, Edward Arnold, 1985. £27.50.

The management of postoperative pain has traditionally been delegated to ward nurses who may give out drugs only at times better suited to off-duty schedules than to patients' needs. They are, in turn, supervised by novice and harassed house surgeons who may have little knowledge of the surgery involved (let alone the analgesics and techniques available), and may then attempt to carry out the orders of anaesthetists, who from lack of inclination or time, may never witness the consequences of their prescriptions. That patients survive the postoperative ordeal is more a tribute to their fortitude than to a team approach for providing satisfactory analgesia. Perhaps surgeons would not embark on painful surgery if they had to manage the pain themselves, and maybe anaesthetists would not so lightly prescribe potent drugs if they were more aware of the consequences?

In this new volume of the *Current Topics in Anaesthesia* series Dr Margaret Dodson sets out, almost single-handed, to provide the information to correct the current mismanagement of postoperative pain. Dr Barbara Pleuvry also added her specialised contributions to the chapters on pharmacokinetics, the pharmacology of analgesic drugs and local anaesthetic drugs while Dr Booker and Dr Nightingale contribute to postoperative analgesia in children. Otherwise, the remaining nine chapters are all written by the principal author.

Virtually every aspect of postoperative pain is covered, referenced and put into perspective. This ranges from psychological preparation to how to conduct a controlled clinical trial on postoperative analgesia, and from acupuncture to patient-controlled analgesia. Omissions relate almost entirely to imminent development, such as the potential for transcutaneous preparations of analgesics.

The reader is lead from discussion of the physiology and psychology of postoperative pain through chapters on pharmacokinetics and pharmacology on to the use of the various drugs. Some will find the occasional lapse into personal observation a welcome diversion from the otherwise meticulous and reasoned consideration of the available data. Each chapter is followed by a comprehensive, accurate and useful list of relevant, up-to-date references. The emphasis on UK practice is illustrated by the lack of mention of sufentanil or USA names for drugs. The proprietary names of systemic analgesic drugs are not given, which is sensible enough in cost conscious Britain, but may reduce the book's value abroad.

The current vogue for intraspinal opioids is extensively and sensibly covered, but thoracic epidural use of local analgesics is scarcely mentioned in the text and not at all in the index, which lacks reference to side effects, vomiting, phantom limb pain, suxamethonium pains or other nonsurgical postoperative pain. Intraspinal morphine is used as the prime example of intraspinal opioids, whereas the other intraspinal opioids are described only in tables. However, the inclusion of nearly 150 references to this topic alone ensures that the interested reader can find ample information.

The young and the elderly receive individual attention, and the problems peculiar to patients with liver, kidney or respiratory diseases are also included. The final chapter on 'The Way Forward', could have provided the basis for defining who is actually to take responsibility for managing the patient's pain, but that thorny problem is evaded. Perhaps postoperative pain 'teams' will eventually develop to anticipate and control postoperative pain, much as the familiar parenteral nutrition teams, but the surgeon, anaesthetist and nurse would then be spared from viewing the results of their own inadequate management. In the meantime, this excellent book will provide much of the necessary information to remove all excuses for failing even to attempt to produce proper postoperative pain relief.

C.E. Blogg

Anaesthesia for Eye, Ear, Nose and Throat Surgery

J.D. Morrison, R.K. Mirakhur and H.J.L. Craig. Pp. 210, Churchill Livingstone, Edinburgh, 1985. £25.00.

This is a second edition. It is perhaps an indication of the increasing complexity which we have introduced into our specialty that we need a book on the subject rather than the time-honoured instructions 'put the tube in the mouth for nasal operations and in the nose for oral operations!'.

Sections are devoted to the nose, the throat, the ear, faciomaxillary injuries and eye operations. There is a presentation of the anatomy of each region, the pathology of related diseases and comments on the common surgical operations undertaken. Anaesthetic techniques are described, as are likely postoperative complications and their anaesthetic implications and management. Each chapter ends with a useful bibliography.

General guidance is given on anaesthesia, local and general, for operations at the head end of the patient. Unfortunately, as the head is attached to the rest of the body, anaesthesia is still complicated by medical problems met in other situations and the authors felt that they had to comment on these as well. The result is a series of very superficial attempts to cover broad topics; the management of diabetes is dealt with in one paragraph! It would have probably been better to recommend to readers that they seek information on such subjects elsewhere. The anatomy sections may be more detailed than is necessary, but at the same time are probably not sufficiently comprehensive for the serious student who should consult a textbook of anatomy.

Some omissions come readily to mind; the only sinus considered is the maxillary sinus and transsphenoidal hypophysectomy does not rate a mention. Comment on the increasing cooperation between ENT surgeons and ophthalmologists with neurosurgeons might also have been expected. However, the book does provide an overview of the subject and provided it is treated in this way, it will be useful for the trainee anaesthetist or the consultant who dabbles only occasionally in these spheres of activity. Much of the text is, and probably has to be, rather repetitive, so it is better not to read the book at one sitting, but rather to dip in and read the sections which relate to a specific problem, more as a reference book than as a text.

W.R. MacRae

Anesthesia for ambulatory surgery

Edited by B.V. Wetchler. Pp. 476, Harper and Row Ltd, 1986. £49.50.

This is a well produced textbook, edited by Dr Bernard V. Wetchler, the Medical Director of the Ambulatory Surgery Center, the Methodist Medical Center of Illinois. There is a need for this book and the editor should be congratulated for selecting 18 expert contributors in the day case surgical field; there are a mixture of hospital doctors, nursing staff and administrators.

The recent report on the *Guidelines for Day Surgery* from the Royal College of Surgeons of England has met with a mixed reception. Wetchler's book, therefore, should be compulsory reading for all enthusiasts and opponents of day surgery. It was refreshing to read in the first chapter that the Americans unashamedly support planned programmes of ambulatory surgery in order to save money for both patients and insurance companies alike. Perhaps this frankness could be matched by many British District Health Authorities with overspending problems this financial year. If day surgery is carefully planned, it can provide a safe, cost effective form of hospital care.

There is no comparable textbook published in Britain. The book has 10 chapters, each giving excellent advice with up-to-date references. Apparently, many American hospitals perform 30 percent of their total surgical workload as day cases. So successful has this been, that there are now 350 free-standing surgical centres throughout the USA. And to think that we in Britain continue to debate the pros and cons of day surgery!

It is acknowledged that American medicine is considerably different from established conservative British practice. However, the chapter on the organisation of a successful day surgical unit will be of especial interest to any British surgeon or anaesthetist asked to establish an effective outpatient surgical service. Detailed information is given on the selection of a site, the constitution of the planning committee and the fundamental requirements for a successful venture.

Naturally, as in any good American book, there is a chapter on legal implications. The importance of good pre-operative patient selection, the performance of appropriate investigations and safe discharge guidelines are repeatedly stressed in this chapter. Interestingly, the American public do not appear to sue their ambulatory surgicenters. When patients are treated as individuals by senior medical staff, the threat of litigation is reduced. However, this chapter on legal matters also discusses office surgery, a model which will, I hope, not be copied in Britain.

There are excellent chapters on the anaesthetic management of paediatric and adult day cases. At the editor's unit, a total of 2951 patients over the age of 60 years were operated upon from 1981–3. The inpatient admission rate from this group of patients was 0.8 percent. As the British geriatric population increases more day surgical facilities for the elderly must surely develop. These patients should be assessed on physiological rather than chronological age.

The chapter on local and regional anaesthesia is most appropriate in a textbook on ambulatory surgery. The Americans perform a great deal of their day surgery under local anaesthesia and this is frequently used for postoperative pain relief. There then follows an informative chapter on the complications after day surgery. The main surgical worry is postoperative haemorrhage, whereas the anaesthetic morbidity is of a minor nature, e.g. nausea, dizziness and headache on return home.

The book is expensive, but I thoroughly recommend it and a copy should be available in every department library. Furthermore, the subject should be brought to the attention of medical students, nurses, surgeons, hospital administrators and district treasurers. For instance, of the ten most commonly performed surgical operations in America, six are done routinely as day cases: biopsy, dilatation and curettage, excision of skin lesions, tubal occlusion, cataract surgery and herniorrhaphy. In the present economic climate, Britain requires imaginative, carefully planned day surgical programmes. The editor of this book is warmly congratulated for the clear and thorough way he has treated his subject.

T.W. Ogg

Cardiac Arrhythmias (Practical Notes on Interpretation and Treatment)

D.H. Bennett. Pp. 194, Wright, 1985. £9.95.

This really is quite a good little book, although it has been written with all junior hospital doctors in mind and not specifically anaesthetists. Its 20 short chapters describe, in simple terms, the main cardiac dysrhythmias, the problems in their interpretation and the practical aspects of their investigation and treatment. It is meant to be read as an introduction to the subject and not as a reference source in which to read up about a particular problem. Given the limited scope it can be recommended as a readable, sensible and clear introduction to the main disturbances of cardiac rhythm. It would be useful to anaesthetists early on in their training, although others may also find it of value. An alteration of cardiac rhythm is quite a common side effect of general anaesthesia. The most common of these disturbances, sinus tachycardia, junctional (nodal) rhythm and ectopic beats, do not usually cause anaesthetists problems in interpretation, but other quite common disturbances do (such as bundle branch blocks). This book may help anaesthetists of all levels of experience, get some of these sorted out.

For an anaesthetic readership there are some obvious shortcomings. Principal amongst these must be the fact that to understand and appropriately treat peri-operative cardiac dysrhythmias, anaesthetists have to understand the underlying causes of a disturbance in cardiac rhythm. For example, to understand why halothane sensitises the heart to catecholamines but isoflurane does not (and may be actually anti-dysrhythmic in certain circumstances), depends on understanding the role of altered conduction velocity in cardiac impulse re-entry. This book does not review the *mechanisms* of cardiac dysrhythmias at all. Indeed, the word re-entry does not appear in the index. In fact, the only entry under R is the Romano-Ward Syndrome, which is congenital prolongation of the Q-T interval; this is indeed of importance to anaesthetists as serious dysrhythmias, including ventricular tachycardia, may occur during anaesthesia. For a review see *Anaesthesia and Intensive Care* 1982; **10:** 50.

This is a good, but in terms of scope, fairly simple and modest book. After I read it I did the quiz at the end of the text and only scored one wrong answer (complete AV block in lead AVR; what looked like P waves were due to somatic tremor because of Parkinson's disease!). This fact says more for the book than any review ever could.

R.M. Jones

Anaesthetic Equipment

C.S. Ward. Pp. 371, Bailliere Tindall, 1985. £22.50.

It is a pleasure to review the second edition of *Anaesthetic Equipment*. The first edition was popular in the UK, mainly because its only rival was American. It was written for anaesthetists, but proved of interest to others involved with our specialty. Because of this, the target readership for this edition has been widened to interest service engineers and technical representatives of the anaesthetic equipment industry.

The book begins, with this audience in mind, with a basic glossary and list of abbreviations. This is followed by an account of physical and mechanical principles, pneumatics and fluidics. The technology of anaesthesia is then described clearly and succinctly, beginning with the supply of medical gases and vacuum systems, continuing with vaporizers, continuous flow and intermittent flow anaesthetic machines, followed by chapters on breathing systems, masks and tracheal tubes.

Manual and automatic ventilators, are discussed but some of the examples are obsolete. This is acknowledged in the preface, because these machines show the principles clearly but the Philips AV-1 and several others are poor choices since very few were sold. The latter part of the book has chapters on humidifiers, monitoring (of anaesthetic machine function), pollution, suction and sterilisation. There is also an interesting section on hazards and the psychology of accidents and electrical safety. In a more administrative vein there are suggestions about anaesthetic room layout, management and organisation of supplies and maintenance.

Many valuable tips and hints are liberally scattered throughout the text and there is a useful address list of suppliers which has some frustrating omissions—where does one obtain a Whistle Discriminator? (Principality Plastics, Rogerstone, Newport, Gwent—*Editor*).

The book should have a wide international readership because equipment for use in the Third World is described in the same detail as that which is used elsewhere. It should be purchased by all trainees.

J.T.B. Moyle

Understanding Anaesthesia Equipment. Construction, Care and Complications (2nd Edition)

J.A. Dorsch and Susan E. Dorsch. Pp. 458, Williams and Wilkins, Baltimore/London, 1984. £49.00.

The text of this new edition fulfils its title but, as with the first edition, it is spoilt by the quality of the illustrations. The contents progress from the supply of medical gases by cylinder and pipeline systems, through anaesthesia machines and vaporizers, breathing systems to masks, airways and tracheal tubes, but there is no mention of automatic ventilators for anaesthesia or of suction apparatus. There are new chapters on controlling trace gas levels, hazards, equipment checking and maintenance (the latter contains a 'cockpit drill'). The equipment is more recognisable to a British reader than that in the first edition, presumably this is a consequence of the take-over of Ohio by British Oxygen.

Most of the chapters begin with a description of the physical principles underlying the components under discussion, but the depth of theory is very variable. The Système Internationale is not used. The description of intermittent flow machines has been eliminated because they are only of historical interest since the last edition, but certain devices, which are still in common use have also disappeared: the Goldman vaporizer, the Boyle's bottle, and the E.M.O. Vaporizer. There is no mention of any apparatus for anaesthesia in the Third World or for military, field anaesthesia.

This book would be recommended if the illustrations were of better quality. There are many good photographs, probably provided by equipment manufacturers, but others are spoilt, for example by using a carpet as a background. Many of the diagrams look as though they are black and white prints from colour transparencies.

This new edition may find a place in the departmental library as a reference text, but cannot be recommended for personal purchase by examination candidates in this country, especially since the 2nd edition of Ward's *Anaesthetic Equipment* has now been published.

J.T.B. Moyle

Monitoring in Anaesthesia and Critical Care Medicine

Edited by C.D. Blitt. Pp. 740, Churchill Livingstone, Edinburgh, 1985. £79.00.

This is an edited book with 35 authors and 28 chapters. According to the editor's preface, the foremost reason for producing the book 'was the need ... for a complete, state of the art text on monitoring, with an emphasis on the fields of anesthesia and critical care medicine'. In addition, 'the book is designed to be a general reference on monitoring'. It is divided into 6 sections: Section 1, General Principles; Section 2, Monitoring the Cardiovascular System; Section 3, Monitoring the Respiratory System; Section 4, Monitoring the Central Nervous System; Section 5, Miscellaneous Monitoring; and Section 6, Monitoring and Subspecialties. The book is strongly bound with an excellent index. The text is arranged in double columns and there are very few typographical errors. The print is clear and, with a few exceptions, the line drawings convey their message well. The standard of photographic reproduction is, however, less commendable and in my copy falls below that which one might expect from a book of this price.

One has come to accept that with edited books there will be a variation in both the standard of content and the style of writing between chapters. This is certainly true here, and in several of the chapters the authors appear to have been given, or to have assumed, a somewhat wider brief than that suggested in the preface. It is, for instance, difficult to justify descriptions of the pharmacology and clinical usage of antidysrhythmic agents, the detailed structure and abnormalities of the haemoglobin molecule, or the physiological changes of pregnancy. It is obvious that these matters are relevant in the choice of physiological variables to monitor, but they could easily have been referred to very briefly with an authoritative source in the references. There are intrusions of this nature in several of the chapters and one found them very distracting in the search for the details of monitoring itself. The degree of repetition is too great to be acceptable: for example, indications for the use of the Swan-Ganz catheter appear in five chapters, and methods of approach to the central veins are described twice.

The book has a wide coverage and, in contrast to other textbooks on monitoring, there seemed to be no omissions of major subjects. The book succeeds to this extent in achieving the objective stated in the preface. All the chapters (apart from one) reach a high standard with respect to the actual information on monitoring and the authors have tried hard to pursue the practical ramifications of their subject matter. There is a sensible selection of figures from original papers to illustrate the arguments of the text, and there are really very few instances where pragmatism replaces a balanced view. The book is outstanding as a source of references and, in contrast to many American textbooks, includes European journals as well.

So, what is this reviewer's conclusion? All aspects of monitoring are considered well, but it would have been a better book had it been half to two-thirds of its present length. The amount of information not directly related to monitoring detracts from its central theme and, although one accepts that each chapter must to a certain extent stand alone, the degree of repetition is excessive. Despite these shortcomings, because of its encyclopaedic nature and the number of references, it is still probably worthwhile for a departmental library.

P. Hutton

1985 Yearbook of Anaesthesia

R.D. Miller, R.R. Kirby, G.O. Ostheimer, L.J. Saidman and R.K. Stoelting. Pp. 395, Year Book, 1985. £41.00.

There are four concerns in a selective précis of the literature. Does it cover a broad field (73 journals)? Are the selection of articles interesting and properly summarised? Are they commented on with punch? Is there any mention of the reviewer's articles? All counts can be answered positively in this book. It is a good selection and the comments are startling at times. The book opens with a chapter on the Informed Anaesthetist. An article on Addiction and Anaesthesiology produces the comment: 'Addiction especially to fentanyl, among anaesthesia residents and faculty is near epidemic in its incidence. It is a major problem on which we need to place great emphasis' (RDM). One must not seem to be complacent, but this is not the case here, in the United Kingdom. Is it just in California? In a Pharmacology Chapter, as a comment on plasma concentrations of catecholamines following adrenaline infiltration there is a new (?) case report of cardiac arrest occurring with an overdose of adrenaline infiltrated with halothane anaesthesia. The circulating nurse is ungallantly (and atypically for the author) and improperly, in my view, blamed in a racy account (GWO). Indeed GWO's commentaries bear study. It must be unwise, although innocuous in this case, to review an article of one's own (RDM) Pharmacokinetics and transfer of vecuronium or from one's own department (RDM and LJS).

The general level is good. The chapters cover a wide spectrum of interests, grouped in subjects such as Anaesthetic Rules, Techniques, Certain Types of Surgery, Monitoring Postoperative Problems, Ventilation, Critical Care and Intraspinal Narcotics. Sometimes the logic in the commentary is suspect or so hedged as to be meaningless. For instance, in references to postoperative pain relief, RKS comments 'Continuous, but appropriately controlled, intravenous infusion of an opioid will eventually, I believe, gain logical acceptance for postoperative analgesia in selected patients'. Hm! No doubt. But what is meant by appropriate and selected?

It is fun to read the commentaries which are often interesting and rarely outrageous. The selections are sufficiently well chosen so that even a diligent clinician would not normally have time to read many in their original. This has always been a good series; this volume is even better. It is a must for every departmental library and bedtime reader.

M. Rosen

A Doctor in Saudi Arabia

G.E. Moloney. Pp. 376, Regency Press, 1985. £12.50.

The cover notes of this book say that the author's reason for writing it was the absence of an equivalent work when he himself was set to depart for Saudi Arabia. The book is intended as an introduction, a scene-setter, to life in Saudi Arabia for expatriate workers, specifically in the field of medicine. Much of the book recounts the author's own experiences anecdotally, but Professor Moloney has tried to choose episodes from his 5-year reign as Professor of Surgery in Riyadh which best illustrate the information the initiate would wish to know.

The book is written in four sections. The first provides an account of the author's arrival in Saudi, and is fairly brief. It prepares the intending traveller in a general way for what to expect from his first exchanges with the local people, whilst not attempting to present a 'checklist'. Things have moved fast in Arabia and doctors travelling on contract to Saudi nowadays have a smoother ride than did Professor Moloney 8 years ago.

The second section is a synopsis of Saudi history and its relevance to present-day Saudi. It includes biographies of the kings of Saudi Arabia and also Lawrence of Arabia, who is apparently the subject of much interest in Saudi. The section includes a most interesting, though compressed part on the twentieth century history of the middle east, though older readers may remember events themselves.

Thirdly, Professor Moloney recounts a selection of tales of his travels within the country. Taken as a whole, this part not only shows the reader the kind of sight which is worth seeing, but also encourages him that such tours are not too difficult to arrange. The author certainly makes light of the discomfort he occasionally suffered during his journeys.

Lastly, the review of Saudi medicine is a useful section for people intending to practice medicine, but also of interest to others. It is written with a minimum of technical terms so that the layman will understand it, and here, as elsewhere, the author demonstrates an ability for rich and colourful description mixed with dry humour. This is well illustrated in a beautiful, poetic description of the pathophysiology of schistosomiasis.

The book is liberally illustrated with black and white photographs, although many of these are very amateur snapshots. Overall, it is an easy book to read, and through the vehicle of describing his own experiences, and by allowing himself to range over any relevant areas of history or medicine at large when appropriate, the author has made the book interesting. It is relatively inexpensive and well worth a leisurely read by anyon with an interest in Saudi Arabia, but who knows littl of the subject.

N. GROVE

Brief Reviews of books received by the Editor

Health Equipment Information No. 153: Evaluation o Resuscitators

A second report has been published about manual adul and child models which includes Aga Revivator, AirViva 11, Ambu Mk III, Flynn, Laerdal Silicone Söhngen 'P', New Sussex Basic and Universal models Vitalograph Rubber and Silicone models and Weinmann Combibag.

Capnography in the operation room: an introductor directory

W.S. MAY JR., J.E. HEAVNER, D. MCWHORTER AND G. RACZ. Pp. 64. Raven Press, 1985. $14.00.

This minute spiral-bound book is Perkin Elmer's answer to the huge atlas of capnography distributed a few years ago by Datex. This one is based solely on the Perkin-Elmer mass spectrometer system which is one o two or three systems currently so popular in the United States. It demonstrates the usual patterns of exhaled carbon dioxide concentrations as tracings and the numerical outputs which, although familiar to all those who have used the system, provide the single best example of the need for the use of a coherent system o units in respiratory physiology.

Anaesthesia, 1986, Volume 41, pages 568–573

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for November 1985. The journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Abdominal surgery

Intraluminal $P\text{CO}_2$: a reliable indicator of intestinal ischemia. Bass, B.L., Schweitzer, E.J. *et al. Journal of Surgical Research* 1985; **39:** 351.

Changes in colonic motility during the development of chronic large bowel obstruction. Coxon, J.E., Dickson, C., Taylor, I. *British Journal of Surgery* 1985; **72:** 690.

Hypovolaemic and healing in colonic anastomoses. Foster, M.E., Laycock, J.R.D. *et al. British Journal of Surgery* 1985; **72:** 831.

A noninvasive method for monitoring intestinal ischemia. Changes in pulmonary clearance of helium instilled in colon as an index of colonic blood flow. Gerstmann, D.R., Waffarn, F. *et al. Pediatric Research* 1985; **19:** 1025.

Studies of the antidiarrhoeal action of clonidine effects on motility and intestinal absorption. Shiller, L.R., Santa, Ana, C.A. *et al. Gastroenterology* 1985; **89:** 982.

Pharmacology

Adrenergic drugs and their antagonists

The effect of isoproterenol on the development and recovery of hypoxic pulmonary hypertension: a structural and hemodynamic study. Fried, R., Reid, L.M. *American Journal of Pathology* 1985; **121:** 102.

The affinity of (-)-propranolol for beta, and beta 2-adrenoceptors of human heart. Gille, E., Lemoine, H. *et al. Naunyn-Schmiedeberg's Archives of Pharmacology* 1985; **331:** 60.

Basic pharmacology of esmolol. Gorczynski, R.J. *American Journal of Cardiology* 1985; **56:** 3F.

Physical performance and serum potassium under chronic beta-blockade. Kullmer, T., Kindermann, W. *European Journal of Applied Physiology* 1985; **54:** 350.

Clinical pharmacology, pharmacodynamics and interactions with esmolol. Lowenthal, D.T., Porter, R.S. *et al. American Journal of Cardiology* 1985; **56:** 14F.

Increased plasma noradrenaline during low dose adrenaline infusion in resting man and during sympathetic stimulation. Musgrave, I.F., Bachmann, A.W. *et al. Clinical and Experimental Pharmacology* 1985; **12:** 285.

Perioperative use of esmolol. Reves, J.G., Flezzani, P. *American Journal of Cardiology* 1985; **56:** 57F.

Current awareness: dopamine and intraocular pressure. Turner, P., Mekki, Q.A. *Trends in Pharmacological Sciences* 1985; **6:** 348.

Increase in $P\text{aO}_2$ following intravenous administration of propranolol in acutely hypoxemic patients. Vincent, J.L., Lignian, H. *et al. Chest* 1985; **88:** 558.

Anaesthetic agents

Endogenous ligands for benzodiazepine recognition sites. Costa, E., Guidotti, A. *Biochemical Pharmacology* 1985; **34:** 3399.

A comparison of the induction characteristics of thiopentone and propofol (2, 6-di-isopropylphenol). Fahy, L.T., Van Mourik, G.A., Utting, J.E. *Anaesthesia* 1985; **40:** 939.

Convulsant component of a depressant benzodiazepine. Garrett, R.L., Bourn, W.M. *Life Science* 1985; **37:** 1933.

Thiobarbiturate-induced histamine release in human skin mast cells. Hirshman, C.A., Edelstein, R.A. *et al. Anesthesiology* 1985; **63:** 353.

Anaphylactoid reactions and histamine by barbiturate induction agents: clinical relevance and patho-mechanisms. Lorenz, W., Doenicke, A. *Anesthesiology* 1985; **63:** 351.

Althesin interaction with human plasma steroid binding globulins. Perrot, D., Pugeat, M. *et al. European*

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London, WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. An exact copy of the monthly section or various cumulative classifications of the Anaesthetic Literature published in the Journal can be obtained on application to him. References from January 1984 have been entered on data base and search facilities are also available. All communications about this matter should be addressed to Dr Kaufman please.

Journal of Clinical Pharmacology 1985; **29:** 181.

Effect of halothane on renal hemodynamics during normovolemia and acute hemorrhagic hypovolemia. Priano, L.L., Marrone, B. *Anesthesiology* 1985; **63:** 357.

Unexplained hepatitis following halothane. Stock, J.G.L., Strunin, L. *Anesthesiology* 1985; **63:** 424.

Analgesic agents

Meptazinol: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic efficacy. Holmes, B., Ward, A. *Drugs* 1985; **30:** 285.

Baclofen prolongs the analgesic effect of fentanyl. Panerai, A.E., Massei, R. *et al. British Journal of Anaesthesia* 1985; **57:** 954.

Naloxone enhances cerebral reactive hyperemia in the rat. Phillis, J.W., De-Long, R.E., Towner, J.K. *Neurosurgery* 1985; **17:** 596.

Muscle relaxants

Neuromuscular transmission and its blockade. Pharmacology, monitoring and physiology updated. Jones, R.M. *Anaesthesia* 1985; **40:** 964.

The influence of physostigmine on visual-vestibular interaction in hereditary ataxias. Tijssen, C.C., Endtz, L.J., Goor, C. *Journal of Neurology Neurosurgery and Psychiatry* 1985; **48:** 977.

Apparatus (equipment, monitoring and measurement)

Laryngeal pacemaker. II. Electronic pacing of re-innervated posterior cricoarytenoid muscles in the canine. Broniatowski, M., Kaneko, S. *et al. Laryngoscope* 1985; **95:** 1194.

Continuous wave doppler determination of right ventricular pressure. A simultaneous doppler-catheterization study in 127 patients. Currie, P.J., Seward, J.B. *et al. Journal of the American College of Cardiology* **6:** 750.

Jet ventilation via a copper endotracheal tube for CO_2 laser surgery of the oropharynx. Herbert, J.T., Berlin, I., Eberle, R. *Laryngoscope* 1985; **95:** 1276.

Electrophysiologic pacing of vocal cord abductors in bilateral recurrent laryngeal nerve paralysis. Otto, R.A., Davis, W. *et al. American Journal of Surgery* 1985; **150:** 447.

Establishment of intravenous lines for long-term intravenous therapy and monitoring. Parsa, M.H., Tabora, F. *Surgical Clinics of North America* 1985; **65:** 835.

Noninvasive intracranial pressure monitoring. Pitlyk, P.J., Piantanida, T.P. *et al. Neurosurgery* 1985; **17:** 581.

Complications

Respiratory complications of gastroesophageal reflux. Barish, C.F., Wu, W.C. *et al. Archives of Internal Medicine* 1985; **145:** 1882.

Extrapyramidal reactions with metoclopramide. Bateman, D.N., Rawlins, M.D., Simpson, J.M. *British Medical Journal* 1985; **291:** 930.

Pathophysiologic characteristics of venous thrombosis. Kakkar, V.V. *American Journal of Surgery* 1985; **150:** 1.

Risk of haemorrhage associated with long term anticoagulant therapy. Levine, M.N., Raskob, G., Hirsh, J. *Drugs* 1985; **30:** 444.

Successful vasoconstrictor therapy of anaphylactoid reactions during induction of anaesthesia. A report of two cases. Ponten, J., Biber, B., Henriksson, B.A. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 639.

Post-traumatic stress disorder from pentaborane. Silverman, J.J., Hart, R.P. *et al. Journal of the American Medical Association* 1985; **254:** 2603.

General anaesthetic procedures

Anesthesiology. Pierce, E.C. *Journal of the American Medical Association* 1985; **254:** 2317.

General interest

Adult respiratory distress syndrome caused by acute systemic lupus erythematosus. Domingopedrol, P., Delaserna, A.R. *et al. European Journal of Respiratory Diseases* 1985; **67:** 141.

Autonomic neuropathy in acute intermittent porphyria. Laiwah, A.C.Y., MacPhee, G.J.A. *et al. Journal of Neurology Neurosurgery and Psychiatry* 1985; **48:** 1025.

Spinal and epidural analgesia

Continuous epidural infusion for analgesia after major abdominal operations—a randomized, prospective, double-blind study. Cullen, M.L., Staren, E.D. *et al. Surgery* 1985; **98:** 718.

Spinal anaesthesia with 0.75-percent bupivacaine and 0.5-percent amethocaine in 5-percent glucose. Marstrand, T., Sorensen, M., Andersen, S. *British Journal of Anaesthesia* 1985; **57:** 971.

Redistribution of lidocaine and bupivacaine after intrathecal injection in mice. Post, C., Freedman, J. *et al. Anesthesiology* 1985; **63:** 410.

The endogenous opioid systems in neurological disorders of the basal ganglia. Sandyk, R. *Life Sciences* 1985; **37:** 1655.

Spinal opioids

Respiratory effects of epidural fentanyl. Ahuja, B.R., Strunin, L. *Anaesthesia* 1985; **40:** 949.

Multiple opiate receptors: functional implications. Dixon, W.R., Viveros, O.H. *et al. Federation Proceedings* 1985; **44:** 2851.

Clinical implications of endogenous opioid peptides. Grossman, A., Clementjones, V., Besser, G.M. *Neuroendocrine Perspectives* 1985; **4:** Ed. Muller E.E. *et al.* (Amsterdam); 243.

Postoperative pain treatment after upper abdominal surgery with epidural morphine at thoracic or lumbar level. Hojkjaer, Larsen, V., Iversen, A.D. *et al. Acta Anaesthesiologica Scandinavica* 1985; **29:** 566.

Recent developments in the bioassay of opioids. Kosterlitz, H.W., Corbett, A.D. *et al. Regulatory Peptides* 1985; Suppl **4:** 1.

Changes in responsiveness to mu and kappa opiates following a series of convulsions. Mansour, A., Valenstein, E.S. *Experimental Neurology* 1985; **90:** 224.

The effects of the acute administration of buprenorphine hydrochloride on release of anterior pituitary hormones in the rat. Pechnick, R.N., George, R., Poland, R.E. *Life Science* 1985; **37:** 1861.

Obstetric anaesthesia and analgesia

Paradoxical response to intravenous terbutaline. Bhat, N., Seifer, D., Hensleigh, P. *American Journal of Obstetrics and Gynecology* 1985; **153:** 310.

Hepatic and peripheral responsiveness to a glucose infusion in pregnancy. Cowett, R.M. *American Journal of Obstetrics and Gynecology* 1985; **153:** 272.

Hemodynamic effects of intravenous hydralazine in pregnant women with severe hypertension. Kuzniar, J., Skret, A. *et al. Obstetrics and Gynecology* 1985; **66:** 453.

Lupus anticoagulant and pregnancy. Lubbe, W.F., Liggins, G.C. *American Journal of Obstetrics and Gynecology* 1985; **153:** 322.

Cardiovascular responses to circulating catecholamines in normal pregnancy and in pregnancy-induced hypertension. Nisell, H., Hjemdahl, P., Linde, B. *Clinical Physiology* 1985; **5:** 479.

Maternal cardiovascular adaptations to twin pregnancy. Veille, J.C., Morton, M.J., Bury, K.J. *American Journal of Obstetrics and Gynecology* 1985; **153:** 261.

Paediatric anaesthesia and intensive care

Evoked fetal startle response: a possible intrauterine neurological examination. Divon, M.Y., Platt, L.D. *et al. American Journal of Obstetrics and Gynecology* 1985; **153:** 454.

Surfactant therapy in the newborn. Leading Article *Lancet* 1985; **2:** 867.

Sleep-waking shifts and cerebral blood flow in stable preterm infants. Greisen, G., Hellstrom-Vestas, L. *et al. Pediatric Research* 1985; **19:** 1156.

Diaphragmatic pacing in infants: techniques and results. Ilbawi, M.N., Idriss, F.S. *et al. Annals of Thoracic Surgery* 1985; **40:** 323.

Ventilatory pattern following diphtheria–tetanus–pertussis immunization in infants at risk for sudden infant death syndrome. Keens, T.G., Davidson, S.L. *et al. American Journal of Diseases of Children* 1985; **139:** 991.

Elevated diaphragm electromyogram during neonatal hypoxic ventilatory depression. Laframboise, W.A., Woodrum, D.E. *Journal of Applied Physiology* 1985; **59:** 1040.

Relation between apnoea duration and type and neurological status of preterm infants. M. Butcher-Puech, D., Henderson-Smart *et al. Archives of Disease in Childhood* 1985; **60:** 953.

Effect of rapid-rate ventilation on the experimental diseased lung caused by meconium aspiration. Obara, H., Maekawa, N. *et al. Biology of the Neonate* 1985; **48:** 149.

Effects of perinatal asphyxia and myoglobinuria on development of acute, neonatal renal failure. Kojima, T., Kobayashi, T. *et al. Archives of Disease in Childhood* 1985; **15:** 908.

Chronic hypoxemia in the newborn lamb—cardiovascular, hematopoietic and growth adaptations. Teitel, D., Sidi, D. *et al. Pediatric Research* 1985; **19:** 1004.

Management of infants with severe respiratory failure and persistence of the fetal circulation, without hyperventilation. Wung, J.T., Lames, L.S. *et al. Pediatrics* 1985; **76:** 488.

Comparison of the effects of barbiturate and ethanol given to neonates on the cerebellar morphology. Yanai, J., Waknin, S. *Acta Anatomica* 1985; **123:** 145.

Cardiovascular system

Physiology

Increased cardiac output increases shunt: role of pulmonary edema and perfusion. Breen, P.H., Schumacker, P.T. *et al. Journal of Applied Physiology* 1985; **59:** 1313.

Calcium antagonism in heart and vascular smooth muscle. Fleckenstein, A. *Medicinal Research Reviews* 1985; **5:** 395.

Pathophysiology of shock-induced disturbances in tissue homeostasis. Haljamae, H. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 38 (suppl).

Role of cardiac and vascular amplifiers in the maintenance of hypertension and the effect of reversal of cardiovascular hypertrophy. Korner, P.I., Jennings, G.L. *et al. Clinical and Experimental Pharmacology and Physiology* 1985; **12:** 205.

Ambulatory electrocardiographic recordings at the time of fatal cardiac arrest. Milner, P.G., Platia, E.V. *et al. American Journal of Cardiology* 1985; **56:** 588.

A circulating myocardial depressant substance in humans with septic shock. Parrillo, J.E., Burch, C. *et al. Journal of Clinical Investigation* 1985; **76:** 1539.

Calcium movements through cardiac cell membranes. Reuter, H. *Medical Research Reviews* 1985; **5:** 427.

Modulation of calcium channel function by drugs. Schramm, M., Towart, R. *Life Sciences* 1985; **37:** 1843.

The pericardial hypothesis—a mechanism of acute shifts of the left ventricular diastolic pressure volume relation. Review. Smiseth, O.A., Kingma, I. *et al. Clinical Physiology* 1985; **5:** 403.

Excitation–contraction coupling and the ultrastructure of smooth muscle. Somlyo, A.P. *Circulation Research* 1985; **57:** 497.

Interaction of cardiopulmonary and carotid baroreflex control of vascular resistance in humans. Victor, R.G., Mark, A.L. *Journal of Clinical Investigation* 1985; **76:** 1592.

Treatment and medication

Nonpulsatile cardiopulmonary bypass disrupts the flow-metabolism couple in the brain. Andersen, K., Waaben, J. *et al. Journal of Thoracic and Cardiovascular Surgery* 1985; **90:** 570.

Common physiologic patterns in general surgical patients—hemodynamic and oxygen transport changes during and after operation. Bland, R.D., Shoemaker, W.C. *Surgical Clinics of North America* 1985; **65:** 793.

Anticoagulant therapy. Coon, W.W. *American Journal of Surgery* 1985; **150:** 45.

Experience with 118 consecutive patients undergoing operations for the Wolff-Parkinson-White syndrome. Cox, J.L., Gallagher, J.J., Cain, M.E. *Journal of Thoracic and Cardiovascular Surgery* 1985; **90:** 490.

Interstitial fluid volume, plasma volume and transcapillary colloid osmotic gradient in patients with hepatic cirrhosis and fluid retention. Fauchald, P., Ritland, S. *Scandinavian Journal of Clinical and Laboratory Investigation* 1985; **45:** 553.

Rationale for the use of colloids in the treatment of shock and hypovolemia. Haljamae, H. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 48 (Suppl).

Difficulties in the treatment of acute pulmonary embolism. Hall, R. *Thorax* 1985; **40:** 729.

The clinical electrophysiology of intravenous indecainide. Horowitz, L.N., Spielman, S.R. *et al. American Heart Journal* 1985; **110:** 784.

Regular review. Calcium channel blocking agents and the heart. Kenny, J. *British Medical Journal* 1985; **291:** 1150.

Intramuscular lidocaine for prevention of lethal arrhythmias in the prehospitalization phase of acute myocardial infarction. Koster, R.W., Dunning, A.J. *New England Journal of Medicine* 1985; **313:** 1105.

Coronary revascularization for recurrent pulmonary edema in elderly patients with ischemic heart disease and preserved ventricular function. Kunis, R., Greenberg, H. *et al. New England Journal of Medicine* 1985; **313:** 1207.

Fresh frozen plasma supplement to massive red blood cell transfusion. Martin, D.J., Lucas, C.E. *et al. Annals of Surgery* 1985; **202:** 505.

A review of the uses and limitations of tocainide—a class IB antiarrhythmic agent. Morganroth, J., Nestico, P.F. *et al. American Heart Journal* 1985; **110:** 856.

Aspects on crystalloid fluid therapy. Mortberg, A. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 45 (Suppl).

Antihypertensive and metabolic effects of nifedipine and labetolol alone and in combination in primary hypertension. Ohman, K.P., Weiner, L. *et al. European Journal of Clinical Pharmacology* 1985; **29:** 149.

Sudden unexpected death in patients with congestive heart failure—a second frontier. Packer, M. *Circulation* 1985; **72:** 681.

Antiarrhythmic drug therapy (part 2). Podrid, P.J. *Chest* 1985; **88:** 618.

Preoperative assessment of high-risk surgical patients. Savino, J.A., Delguercio, L.R.M. *Surgical Clinics of North America* 1985; **65:** 763.

Calcium-antagonist drugs: receptor interactions that clarify therapeutic effects. Snyder, S.H., Reynolds, I.J. *New England Journal of Medicine* 1985; **313:** 995.

Perioperative anesthetic risk of noncardic surgery in hypertrophic obstructive cardiomyopathy. Thompson, R.C., Liberthson, R.R., Lowenstein, E. *Journal of the American Medical Association* 1985; **254:** 2419.

Sodium bicarbonate during CPR: does it help or hinder? Weil, M.H., Trevino, R.P., Rackow, E.C. *Chest* 1985; **88:** 487.

Respiration

Physiology

Factors affecting the decline of ventilatory function in chronic bronchitis. Campbell, A.H., Barter, C.E. *et al. Thorax* 1985; **40:** 741.

Sympathetic rhythms during hyperventilation-induced apnea. Connelly, C.A., Wurster, R.D. *American Journal of Physiology* 1985; **249:** R424 (part 2).

Rib cage mechanics in simulated diaphragmatic paralysis. Detroyer, A., Estenne, M., Ninane, V. *American Review of Respiratory Disease* 1985; **132:** 793.

Effect of inspiratory muscle fatigue on breathing pattern. Gallagher, C.G., Hof, V.I., Younes, M. *Journal of Applied Physiology* 1985; **59:** 1152.

Oxidant gas injury to the lung: a discussion on the functional implications. Guidotti, T.L. *Journal of Applied Toxicology* 1985; **5:** 320.

Lung surfactant and pulmonary toxicology. Haagsman, H.P., Van Golde, L.M.G. *Lung* 1985; **163:** 275.

Steady-state response of conscious man to small expiratory restive loads. Hill, A.R., Kaiser, D.L. *et al. Respiration Physiology* 1985; **61:** 369.

Prolonged expiratory apnoea and implications for control of breathing. Johndon, P. *Lancet* 1985; **2:** 877.

Transmission of airway pressure to pleural space during lung edema and chest wall restriction. O'Quin, R.J., Marini, J.J. *et al. Journal of Applied Physiology* 1985; **59:** 1171.

Independently measured oxygen consumption during reduction of oxygen delivery by positive end-expiratory pressure. Pepe, P.E., Culver, B.H. *American Review of Respiratory Disease* 1985; **132:** 788.

Maximal inspiratory and expiratory pressures are reduced in hyperinflated, malnourished, young adult male patients with cystic fibrosis. Szeinberg, A., England, S. *et al. American Review of Respiratory Disease* 1985; **132:** 766.

Pulmonary function and ventilatory response to chemical stimuli in familial myopathy. Weng, T.R., Schultz, G.E. *et al. Chest* 1985; **88:** 488.

Respiration

Treatment and medication

Combined salbutamol and ipratropium bromide by inhalation in the treatment of severe acute asthma. Beck, R., Robertson, C. *et al. Journal of Pediatrics* 1985; **107:** 605.

Hemodynamic effects of inhaled ipratropium bromide, alone and combined with an inhaled beta 2-agonist. Chapman, K.R., Smith, D.L. *et al. American Review of Respiratory Disease* 1985; **132:** 845.

Assisted ventilation in patients with pre-existing cardiopulmonary disease. Chin, W.D.N., Cheung, H.W. *et al. Chest* 1985; **88:** 503.

Inspiratory work and airway pressure with continuous positive airway pressure. Katz, J.A., Kraemer, R.W., Gjerde, G.E. *Chest* 1985; **88:** 519.

High-frequency jet ventilation. Klain, M., Keszler, H. *Surgical Clinics of North America* 1985; **65:** 917.

Controversies in the pathophysiology and fluid management of postoperative adult respiratory distress syndrome. Shoemaker, W.C. *Surgical Clinics of North America* 1985; **65:** 931.

Central nervous system

Physiology

Cerebral norepinephrine depletion enhances recovery after brain ischemia. Busto, R., Harik, S.I. *et al. Annals of Neurology* 1985; **18:** 329.

Cerebral blood flow, metabolic rate and cross-brain oxygen consumption in brain injury. Frewen, T.C., Sumabat, W.O., Delmaestro, R.F.D. *Journal of Pediatrics* 1985; **107:** 510.

Receptor–receptor interactions in the central nervous system. A new integrative mechanism in synapses. Fuxe, K., Agnati, L.F. *Medicinal Research Reviews* 1985; **5:** 441.

Cerebral infarction in sickle cell trait. Greenberg, J., Massey, E.W. *Annals of Neurology* 1985; **18:** 354.

Brain blood volume and blood flow in patients with plateau waves. Hayashi, M., Kobayashi, H. *et al. Journal of Neurosurgery* 1985; **63:** 556.

Oxygen radicals in cerebral vascular injury. Kontos, H.A. *Circulation Research* 1985; **57:** 508.

The cerebral venous system. Schmidek, H.H., Auer, L.M., Kapp, J.P. *Neurosurgery* 1985; **17:** 663.

Alterations of regional cerebral blood flow and oxygen metabolism in Parkinson's disease. Wolfson, L.I., Leenders, K.L. *et al. Neurology* 1985; **35:** 1399.

Treatment and medication

Safe use of PEEP in patients with severe head injury. Cooper, K.R., Boswell, P.A., Choi, S.C. *Journal of Neurosurgery* 1985; **63:** 552.

The treatment of Parkinson's disease. Morris. J.G.L. *Medical Journal of Australia* 1985; **143:** 347.

Hemodilution in acute stroke. Thomas, D.J. *Stroke* 1985; **16:** 763.

Endocrine and metabolic

Physiology

Increased insulin responsiveness and insulin clearance in thyrotoxicosis. Barzilai, N., Cohen, P. *et al. Israel Journal of Medical Sciences* 1985; **21:** 722.

Spurious assessment of acid-base status due to dilutional effect of heparin. Bloom, S.A., Canzanello, V.J. *et al. American Journal of Medicine* 1985; **79:** 528.

A vasopressin-mediated diminution of potassium excretion in water-loaded man. Buckley, J., Gebruers, E.M. *et al. Clinical Science* 1985; **69:** 601.

Effects of oxytocin and vasopressin in the central and in the autonomic nervous system—interactions with other presumptive neurotransmitters. Dreifuss, J.J., Kiraly, M. *et al. Regulatory Peptides* 1985; Suppl **4:** 165.

Effect of head-down tilt on basal plasma norepinephrine and renin activity in humans. Goldsmith, S.R., Francis, G.S., Cohen, J.N. *Journal of Applied Physiology* 1985; **59:** 1068.

Importance of endogenous vasopressin in the hypertensive and bradycardiac response to central alpha-adrenergic stimulation. Hiwatari, M., Johnston, C.I. *Clinical and Experimental Pharmacology and Physiology* 1985; **12:** 221.

Renal responses to stressful environmental stimuli. Koepke, J.P. *Federation Proceedings* 1985; **44:** 2823.

Renorenal reflexes: neural and functional responses. Kopp, U.C. *Federation Proceedings* 1985; **44:** 2834.

The influence of surgical operations on components of the human immune system. Lennard, T.W.J., Shenton, B.K. *et al. British Journal of Surgery* 1985; **72:** 771.

Cardiopulmonary blood volume and plasma renin activity in normal and hypertensive humans. London, G.M., Guerin, A.P. *et al. American Journal of Physiology* 1985; **249:** H807 (part 2).

Pathophysiology of protracted acute renal failure in man. Moran, S.M., Myers, B.D. *Journal of Clinical Investigation* 1985; **76:** 1440.

Effects of epidural analgesia on plasma catecholamines and cortisol in parturition. Neumark, J., Hammerle, A.F., Biegelmayer, C. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 555.

Ventilatory and metabolic effects of glucose infusions. Rodriquez, J.L., Askanazi, J. *et al. Chest* 1985; **88:** 512.

Clinical effects of altered vasopressin secretion. Vokes, T., Robertson, G.L. *Neuroendocrine Perspectives* 1985; **4:** Ed. Muller E.E. *et al.*, (Amsterdam); 1.

Treatment and medication

Resistance to loop diuretics: why it happens and what to do about it. Brater, D.C. *Drugs* 1985; **30:** 427.

Effect of furosemide on urinary excretion of 4-hydroxy-3-methoxymandelic acid. Bursztyn, M., Gutman, A. *Israel Journal of Medical Sciences* 1985; **21:** 742.

Significant metabolic acidosis induced by acetazolamide. Heller, I., Halevy, J. *et al. Archives of Internal Medicine* 1985; **145:** 1815.

Influence of diabetes mellitus on operative risk. Hjortrup, A., Sorensen, C. *et al. British Journal of Surgery* 1985; **72:** 783.

Hormonal blockade modifies post-traumatic protein catabolism. Hulton, N., Johnson, D.J. *et al. Journal of Surgical Research* 1985; **39:** 310.

Effects of vasopressin antagonist on vasopressin binding, adenylate cyclase activation and water flux. Kim, J.K., Dillingham, M.A. *et al. Journal o Clinical Investigation* 1985; **76:** 1530.

Adrenal corticosteroid replacement therapy. Mortimer, R.H. *Medical Journal of Australia* 1985; **143:** 350.

Haemodynamic effects of low and high doses of insulin during beta-receptor blockade in dogs. Reikeras, O., Gunnes, P. *et al. Clinical Physiology* 1985; **5:** 455.

Metabolic effects of low and high doses of insulin during beta-blockade in dogs. Reikeras, O., Gunnes, P. *et al. Clinical Physiology* 1985; **5:** 469.

Use of furosemide in the evaluation of renal tubula acidosis. Stine, K.C., Linshaw, M.A. *Journal o Pediatrics* 1985; **107:** 559.

Hypertension corrected and aldosterone responsivenes to renin-angiotensin restored by dexamethasone i glucocorticoid-suppressible hyperaldosteronism. Woodland, E., Tunny, T.J. *et al. Clinical an Experimental Pharmacology and Physiology* 1985; **12** 245.

Pain

Physiology

Shock controllability and the nature of stress-induced analgesia. Drugan, R.C., Ader, D.N., Maier, S.F. *Behavioral Neuroscience* 1985; **99:** 791.

Chronic pain—lifetime psychiatric diagnoses and family history. Katon, W., Egan, K., Miller, D. *American Journal of Psychiatry* 1985; **142:** 1156.

Other

Physiology

Studies on the pharmacological control of gastric emptying in man. Bateman, D.N. *British Journal o Clinical Pharmacology* 1985; **20:** 339.

Anaesthesia, 1986, Volume 41, page 574

Safety Information Bulletin

These are issued by the Department of Health and Social Security

Defibrillators with earth referenced outputs: risk of electric shock to operators

Some old models of defibrillator may, by design, have one side of their output connected to earth or to accessible conductive parts. This increases the risk of electric shock to any person who touches a patient during defibrillation. These defibrillators should be withdrawn from service. A list of models which do *not* have this short coming in their design is given in the Appendix to Safety Information Bulletin No. 26: SIB(86)5. Most models supplied since 1975 are probably satisfactory.

Stop Press

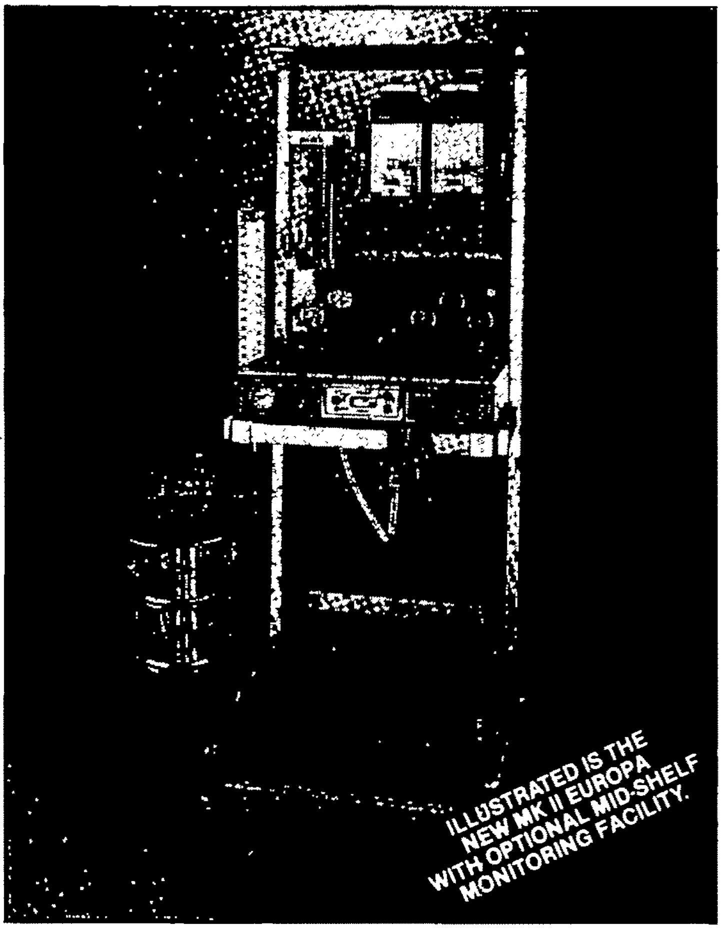
National and local event

May 9 1986

Society of Naval Anaesthetists Plymouth Postgraduate Medical Centre.
Theme—ImmediateCare.

Information: Dr A. Yates, Royal Naval Hospital, Plymouth PL1 3JY.

'EUROPA' ANAESTHETIC EQUIPMENT


ILLUSTRATED IS THE NEW MK II EUROPA WITH OPTIONAL MID-SHELF MONITORING FACILITY.

Built to high standards of design and finish, the Tricomed EUROPA is able to provide the most comprehensive specification demanded in modern anaesthesia.

TRIcoMED®

Tricomed Limited, 5-7 Sydenham Road, London, SE26 5ET, England.
Telephone 01-778 1165 Telex 8955141 TRIMED

Tricomed Pty Limited, 21 Shepherd Street, Marrickville, NSW 2204,
Australia. Telephone 2 569 1585

Tricomed (Hong Kong) Limited, 905 Car Po Commercial Building,
18 Lyndhurst Terrace, Central, Hong Kong. Tel: 5 442989 Tlx: 64078 TRIMD.HX

AErrane™ (isoflurane)

A Complete Anaesthetic

- With or without premedications, relaxants or nitrous oxide, AErrane™ (isoflurane) suppresses consciousness, pain, muscle tone, and memory of the operation.
- Inhalational control is enhanced by a low solubility in blood.
- Muscle relaxation with AErrane™ (isoflurane) alone is sufficient for most surgical needs; supplemental relaxant requirement is markedly reduced or eliminated (as is the need for reversal agents postoperatively).
- Relaxation of the chest wall and diaphragm permits easily assisted or controlled ventilation without concern for "stiff chest." Respiratory depression dissipates promptly with recovery.
- AErrane™ (isoflurane) is the most rapidly eliminated of all potent modern anaesthetics,[1] thus providing for a prompt, smooth recovery with few post-anaesthetic sequelae.

Please contact your Anaquest representative or our offices to arrange for AErrane™ (isoflurane) vaporisers.

AErrane™...a product of original Anaquest research (isoflurane)

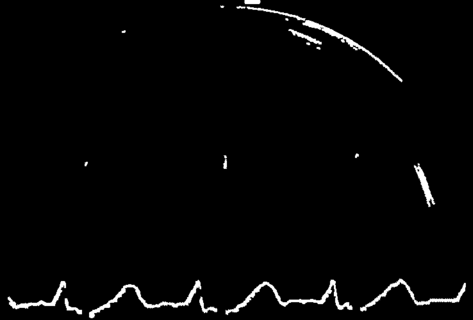
Anaquest

[illegible]
[illegible]
[illegible]
United Kingdom
[illegible]

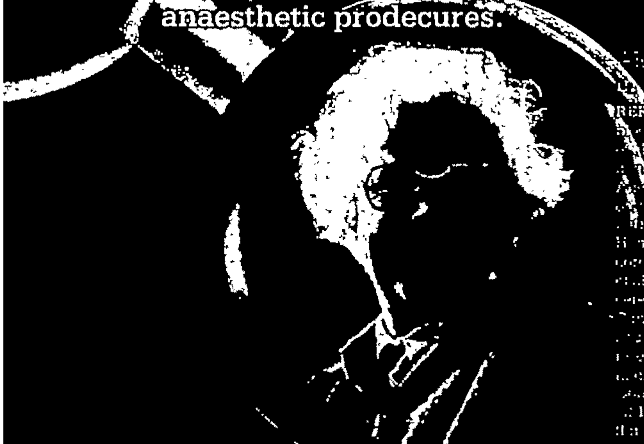
[illegible] Road
Sandyford Industrial Estate
Dublin [illegible] Ireland
[illegible]

For the Sum of Your Patient's Anaesthetic Needs

Intraoperative Margins of Safety



- AErrane™ (isoflurane) causes a dose-related decrease in peripheral resistance (and cardiac afterload) but little or no depression of myocardial function or cardiac output (at normal levels of surgical anaesthesia, 1 to 1.5 MAC).[1] These effects are potentially useful in the elderly,[2] in patients with coronary artery disease,[3] and for induced hypotension in cerebral aneurysm surgery.[5]
- **Cardiac rhythm tends to remain stable.** A report from a large multi-centre study of 6,798 patients states, "In none of the extensive analyses did isoflurane itself appear to be a factor associated with development of arrhythmias."[6] AErrane™ (isoflurane) also does not increase myocardial sensitivity to adrenalin[7] used for haemostasis or to endogenous catecholamines.[4]
- **An excellent choice for neurosurgery.** AErrane™ (isoflurane) causes no increase in intracranial pressure (ICP) when $PaCO_2$ is controlled at 25-30 mmHg.[9] ICP is readily lowered at any time by decreasing $PaCO_2$ (convulsive activity is not seen at any $PaCO_2$ level or anaesthetic concentration).
- **AErrane™ (isoflurane) is the least metabolized of all potent anaesthetics.**
- **AErrane™ (isoflurane) has been used in more than 20 million anaesthetic prodecures.**



AErrane™ (isoflurane) is not approved for [illegible]

REFERENCES: [illegible]

Prescribing Information. Indications: [illegible] **Dose:** [illegible] **Contraindications:** [illegible] **Side Effects:** [illegible] **Product Licence Number:** [illegible]

Announcing the new third edition of

OBSTETRIC ANAESTHESIA AND ANALGESIA

by Donald D. Moir & John Thorburn

- extensively revised and completely up-to-date
- an invaluable practical guide

This well-established text covers all aspects of the subject in an informative and readable way. Of special interest are the new sections on the control of gastric acidity, failed or difficult intubation, epidural anaesthesia for caesarian section, spinal anaesthesia in obstetrics and the effects of anaesthesia on placental blood flow, plus information on new regimens and alternative positions for labour and delivery. The book is intended for anaesthetists in training, especially candidates for the FFARCS, and for their senior colleagues who administer obstetric anaesthesia and analgesia.

0 7020 1154 1 390pp Ills Hb Baillière Tindall (UK) February 1986 £17.95

for complementary reading . . .

ACTIVE MANAGEMENT OF LABOUR (2/e)

by K. O'Driscoll & D. Meagher

". . . To read this book with its unique approach will be a stimulating and exhilarating experience . . ."

SOUTH AFRICAN MEDICAL JOURNAL *(from a review of the previous edition)*

The second edition of this practical account of the Dublin system of the management of labour includes new material on caesarian section and completely updated statistics and tables.

0 7020 1159 2 ca 224pp ca 34 ills Hb Baillière Tindall (UK) March 1986 £9.95

Also recently published . . .

DIFFICULTIES IN TRACHEAL INTUBATION

by I. P. Latto & M. Rosen

A comprehensive survey of tracheal and endobronchial intubation techniques, coupled with extensive practical advice on solving problems that may be encountered. Profusely illustrated and with extensive referencing, the book will appeal to both the experienced anaesthetist and the candidate for the higher examinations.

0 7020 1096 0 192pp 150 ills Hb
Baillière Tindall (UK) 1985 £14.50

ANAESTHETIC EQUIPMENT (2/e)

by C. S. Ward

A practical text offering advice on the operation and maintenance of equipment, as well as how to cope with common causes of mechanical failure. It will be invaluable to both trainee and established anaesthetists wishing to obtain a thorough understanding of the equipment used in anaesthetic practice.

0 7020 1008 1 384pp 460 ills Hb
Baillière Tindall (UK) 1985 £22.50

ORDERING INSTRUCTIONS

These books are available through booksellers, but in case of difficulty, complete the order form and send it, with your payment, to:
Baillière Tindall/W. B. Saunders, 1 St Anne's Road, Eastbourne, East Sussex BN21 3UN, England.
Prices, specifications and availability are subject to change without notice.
Postage and Packing/Handling Charges. *UK & Eire:* Prices quoted for books include postage and packing/handling charges for delivery within the UK & Eire. *Europe:* Please add £2.50 for the first book and £0.75 for each additional book ordered. **Rest of the World:** Please add £5.00 for the first book and £1.50 for each additional book ordered. Books are despatched by air-speeded methods, but please allow a minimum of 28 days for delivery overseas.

BAILLIÈRE TINDALL
W. B. SAUNDERS

Registered Office: Holt-Saunders Ltd, 1 St Anne's Road, Eastbourne,
East Sussex BN21 3UN, England. Registration No. 157437.
Telephone: Eastbourne (0323) 638221. Telex: 877503 Volmst.

Return to **Baillière Tindall/W. B. Saunders, 1 St Anne's Road, Eastbourne, East Sussex BN21 3UN, England**

Please send me the following books:

☐ 0 7020 1154 1 Obs Anaes/Analg (3/e) £17.95
☐ 0 7020 1159 2 Actv Mgt Labour (2/e) £9.95
☐ 0 7020 1096 0 Dffclts Trach Intbtn £14.50
☐ 0 7020 1008 1 Anaes Equpmt (2/e) £22.50

I enclose £.................. in payment for book(s) ordered, plus £.................. for postage and packing/handling charges as applicable *(see ordering instructions for details)*.

METHODS OF PAYMENT

I enclose £.................. being payment by:
(please tick)

☐ cheque *(payable to Holt-Saunders Ltd)*
☐ eurocheque ☐ sterling bank draft
☐ Access ☐ American Express
☐ Diners Club ☐ Visa *(except France)*

Credit Card No: ....
Expiry date ....

NAME (please print) ....
ADDRESS ....
....
....
Postcode.................................. Country ....
DAYTIME TELEPHONE NO: ....
SIGNATURE.................................. Date ....

EBCAAB80

Anaesthesia and Intensive Care

CONTENTS

COVERNOTE

EDITORIAL

COMPUTER-CONTROLLED MUSCLE PARALYSIS WITH ATRACURIUM IN THE SHEEP, D G Lampard, W A Brown, N M Cass, K C Ng

REDUCTION OF HEAT LOSS DURING TRANSURETHRAL RESECTION OF THE PROSTATE, P M Dyer, P S Heathcote

CLINICAL OBSERVATIONS ON THE PATHOPHYSIOLOGY AND TREATMENT OF ANAPHYLACTIC CARDIOVASCULAR COLLAPSE, M McD Fisher

THIOPENTONE CEREBRAL PROTECTION UNDER EEG CONTROL DURING CAROTID ENDARTERECTOMY, R G Hicks, D R Kerr, D A Horton

UNEXPLAINED ACUTE MEMBRANE PULMONARY OEDEMA RELATED TO ANAESTHESIA, M McD Fisher, I F Stevenson

COMPUTERISED EEG MONITORING FOR CAROTID ENDARTERECTOMY, A B Baker, A J Roxburgh

ALFENTANIL FOR SHORT DURATION LAPAROSCOPIC PROCEDURES, K S Lee, G J Purcell, B R Rae, B White

POSTOPERATIVE NEUROMUSCULAR FUNCTION, G H Beemer, P Rozental

REVIEW

Extracorporeal CO_2 Removal in Severe Adult Respiratory Distress Syndrome, K G Hickling

Pulmonary Oedema Following Acute Upper Airway Obstruction, E S Barin, I F Stevenson, G L Donnelly

EQUIPMENT

A Comparative Study of the Measurement of Mean Arterial Blood Pressure Using Automatic Oscillometers Arterial Cannulation and Auscultation, A J Rutten, A H Ilsley, G A Skowronski, W B Runciman

The Combibag: An Evaluation of a New Self-Inflating Resuscitator, T Cramond, J P O'Callaghan

HISTORY OF ANAESTHESIA

Surgery Without Pain – Part 1: Background, W D A Smith

CASE REPORTS

Management of Severe ARDS With Low Frequency Positive Pressure Ventilation and Extracorporeal CO_2 Removal, K G Hickling, G Downward, F M Davis, G A'Court

Computed Tomography Scanning in Acute Pulmonary Problems, A S McLean

Bilateral Block of Cervical and Brachial Plexuses Following Interscalene Block, K C Huang, M R FitzGerald, K Tsueda

Published quarterly by the Australian Society of Anaesthetists

1986 Subscription: $Aust 34.00 Editor: Dr B F Horan

Address for correspondence: PO Box 600, EDGECLIFF, NSW 2027, Australia

Canadian Anaesthetists' Society Journal

SUBSCRIBE

A highly regarded international anaesthesia journal publishing reports of current investigations, informative review articles, editorials, clinical and technical reports, book reviews, correspondence, and meeting notices. Published bi-monthly in January, March, May (Parts I and II), July, September, and November (includes Index of Authors and Index of Subjects).

Each journal issue contains a Continuing Medical Education Section provided in rotation by Canadian university Departments of Anaesthesia. The CME section summarizes clinically relevant information intended for all anaesthetic practitioners.

The Annual Meeting Supplement produced as Part II of each May issue contains Refresher Course Outlines and abstracts of papers presented in the Scientific Programme of the Annual Meeting of the Canadian Anaesthetists' Society held in June of each year.

Canadian Anaesthetists' Society Journal
Journal de la Société Canadienne des Anesthésistes

CME Topics Scheduled for 86

Anaesthesia Breathing Circuits

Up-date on Obstetrical Anaesthesia

Anaesthesia & Allergic Drug Reactions

Choice of Monitoring Equipment in Anaesthesia & Intensive Care

Myocardial Infarction & Anaesthesia

Management of Chronic Pain

ORDER FORM

Please enter my subscription for the Canadian Anaesthetists' Society Journal

Commencing:
month __________ year 198_

1986 Subscription Rates: (Canadian Dollars)

☐ Individual	$57.50
☐ Institutional	$80.00
☐ Air Mail (optional)	$35.00

☐ Payment enclosed or
☐ Bill to my Credit Card Account Number __________________ Visa ☐ MasterCard ☐

Signature ________________ Expiry Date ________

Please make remittance payable to and mail to:
Canadian Anaesthetists' Society Journal
94 Cumberland Street, Suite 901, Toronto, Ontario, Canada, M5R 1A3 (416) 923-1449

(Please Print)

Name: ________________ Date ________

Address: ________________ Postal/Zip Code ________

Notice to contributors to *Anaesthesia*

Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Articles accepted become copyright of *Anaesthesia*.

Contributors are requested to submit two copies of manuscripts. They are also advised to retain a third copy as the Editors cannot accept responsibility for the loss of manuscripts in the post. The covering letter should be signed personally by all the authors and careful consideration should be given to the decision to include more than five authors. Articles should be forwarded to:

Dr J. N. Lunn, Editor of ***Anaesthesia****, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.*

PREPARATION OF MANUSCRIPTS

Articles for *Anaesthesia* should be prepared in accordance with *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5) except that the titles of journals in the reference section should be given in full (see below). A reprint of these requirements of which this notice is a summary, can be obtained from the *British Medical Journal* price 50 pence (U.K.).

Type manuscripts on white bond paper, 20.3 × 26.7 cm or 21.6 × 27.9 cm (8 × 10½ in. or 8½ × 11 in.) or ISO A4 (212 × 297 mm) with margins of at least 2.5 cm (1 in.). Use double, and preferably triple, spacing throughout, including the references. Please do not use a dot matrix printer, particularly one with poor quality descenders or ascenders. Unseparated, fan-folded manuscripts may be returned to the author.

The manuscript should consist of the following sections in this order each beginning on a new page: *title page, summary* and *key words, text, acknowledgments, references, individual tables,* and *legends for figures.*

Number pages consecutively, beginning with the title page. Type the page number in the upper right-hand corner of each page.

THE TITLE PAGE

The name of the author and the address to which proofs and other correspondence is to be addressed should appear in the top left-hand corner of the sheet.

The main title should be restricted to five words if this is possible. It should be typed in capitals across the centre of the title page.

A subsidiary title of not more than 12 words may be supplied if this is considered to be necessary. This should be typed in lower case immediately beneath the main title.

The names of the authors should be typed IN CAPITALS across the title page immediately beneath the titles without degrees or designations. Initials should precede the surname. One forename may be given in full according to the author's preference. If there is more than one author the word 'AND' should be placed before the name of the last author.

A line should be typed across the title page below the author(s) name(s) in capitals.

The author(s) name(s) degrees and designations should be typed in lower case below the line. Initials and/or forename should precede the name of each author and his degrees, without full stops between letters, and appointment (e.g. Consultant, Registrar, etc.) should follow it.

A full postal institutional address should follow the names, degrees and appointments. Correspondence will normally be addressed to the first author but, if it is desired to direct correspondence other than to the first author, or if different authors belong to different institutions or departments, a separate sentence should be added; this should start on a new line and begin 'Correspondence should be addressed to . . .' and a full postal address should follow.

SUMMARY AND KEY WORDS

Start a new sheet

The second page should carry a summary of not more than 150 words. The summary should state the purpose of the study or investigation, basic procedures, main findings and their statistical significance, and the principal conclusions.

Do not use abbreviations except for units of measurement (e.g. mg, cm, etc.).

Key (indexing) words. Below the abstract, provide and identify as such, three to 10 key words or short phrases that will assist indexers. Use terms from the Medical Subject Headings list from *Index Medicus.* The Editor may modify these at proof stage to conform with agreed practice of certain other anaesthetic journals in the English language.

COPYRIGHT OFFPRINTS

Authors submitting a manuscript do so on the understanding that if it is accepted for publication, exclusive copyright in the paper shall be assigned to the Association. In consideration for the assignment of copyright, the Publisher will supply 25 offprints of each paper. Further offprints may be ordered at extra cost; the copyright assignment form and the offprint order form will be sent with the proofs. The Association will not put any limitation on the personal freedom of the author to use material contained in the paper in other works.

(*continued overleaf*)

THE TEXT

Start a new sheet

The text of observational and experimental articles, case reports, etc. is usually divided into section
the headings *Introduction, Methods, Results* and *Discussion.* Long articles will need subheadings
some sections to clarify their content.

Letters for the correspondence pages should be double spaced and prepared in accordance wi
format in a recent copy of *Anaesthesia.*

Headings: three steps of heading may be used in typescripts:

(i) CAPITALS across the centre of the page.
(ii) Underlined words
These should be typed at the left hand side of the page above the paragraph which they pr
(iii) Underlined words at the beginning of a paragraph. These may either be followed by a ful
or form part of the first sentence of the paragraph.

ACKNOWLEDGMENTS

Start a new sheet

Acknowledge those who have made substantive contributions to the study or the preparation
manuscript. Authors are responsible for obtaining written permission for publication of repro
figures and tables from authors and publishers and from everyone acknowledged by name beca
copyright conventions and because readers may infer their endorsement of the data and conclusio

REFERENCES

Start a new sheet

Number references consecutively in the order in which they are first mentioned in the text. Id
references in text, tables and legends by arabic numerals. References cited only in tables or in le
to figures should be numbered in accordance with a sequence established by the first identificati
the text of the particular table or illustration. Use double or treble space typing.

Use the form of reference adopted by the U.S. National Library of Medicine and used in
Medicus. Use the style of the examples cited at the end of this section.

The titles of journals should be given in full.

Avoid using abstracts as references except those published in a recognised journal. 'Unpub
observations' and 'personal communications' may not be used as references, although references to w
not verbal, communications may be inserted (in parentheses) in the text. Include among the refe
manuscripts accepted but not yet published; designate the journal followed by (*in press*) in parent
Information from manuscript submitted but not yet accepted should be cited in the text as (unpub
observations) in parentheses.

The references must be verified by the author(s) against the original documents.

Examples of correct form of references

Note: first and last pages in all references.

JOURNAL

Standard journal article—(List all authors)

Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamin
eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Me*
1976; **294:** 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physi
Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandi*
Journal of Clinical Laboratory Investigation 1976; **36:** 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:**

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

Osler AG. *Complement: mechanisms and functions.* New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. AMA drug evaluations. 3rd ed. New York: Publ
Sciences Group, 1977.

Editor, compiler, chairman as author

Rhodes AJ, Van Rooyen CE, *comps. Textbook of virology: for students and practitioners of me*
and other health sciences. 5th ed. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

Weinstein L, Swartz MN Pathogenic properties of invading micro-organisms. In: Sodeman W
Sodeman WA, eds. *Pathologic physiology: mechanisms of disease.* Philadelphia: WB Saunders,
457–72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, U
States, July 1968—June 1969. Rockville, Md: National Center for Health Statistics, 1972. (*Vita*
health statistics. Series **10:** Data drom the National Health Survey. No. 69) [DHEW publicatio
(HSM) 72–1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

ROUECHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

TABLES

Do not include tables in the text. Start a new sheet for each table and space the material adequately. The author(s) name(s) should appear in the top right-hand corner.

Indicate the approximate position of each table in relation to the subject matter of the text in the right-hand margin of the appropriate page on the manuscript. Do not submit tables as photographs. Number tables consecutively with arabic numerals. Supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes. Explain in footnotes all non-standard abbreviations that are used in each table. For footnotes, use the following symbols in this sequence: *, †, ‡, §, ||, ¶, **, ††, etc. Identify statistical measures of variations such as SD and SEM. *Legends for tables* should appear on the face of the table.

Cite each table in the text in consecutive order and mark the approximate position of the table in the right-hand margin of the text.

FIGURES

Each figure should be separate. Do not include figures in the text but collect together in an envelope or folder.

Indicate the approximate position of each figure in relation to the subject matter of the text in the right-hand margin of the appropriate page of the manuscript. Drawings, charts and diagrams should be submitted in black indian ink on a smooth white card and should be about twice the size of that desired in the published version with no lettering. Full plate, glossy black and white photographs will be accepted if they are sufficiently clear. All letters and numerals required on the face of figures must be clearly typed or written on tracing paper firmly attached with self-adhesive tape to the back of the figure and folded over from the front as a cover. They will then be printed in the style of *Anaesthesia* in the exact location indicated. Identify each figure by its sequential number in pencil on the reverse of the illustration and include the title of the paper and the authors' names. Mark the top of the illustration on the reverse by an arrow and the word 'Top'.

All sources of identification of patients must be removed.

LEGENDS FOR FIGURES

Start a new sheet

Type legends for illustrations double spaced with arabic numerals corresponding to the illustrations. When symbols, arrows, numbers or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

CONVENTIONS AND ABBREVIATIONS

Statistics and measurements should be given in figures except that numerals one to nine should be in words if not followed by a measurement symbol (e.g. 'two patients' but '2.0 mg'). The *Système International* (SI) will usually be used except that vascular pressures will be recorded in mmHg and cmH_2O. Imperial measurements will not be used except in an historic context. The 24 hour clock will be used.

Contributors are advised to study the SI *Conversion Tables* provided in the January 1978 issue of *Anaesthesia*, *Units, Symbols and Abbreviations* (*A Guide for Biological and Medical Editors and Authors*) published by the Royal Society of Medicine, London W1M 8AE, and *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5).

LETTERS FOR PUBLICATION

Should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University of Wales Hospital, Heath Park, Cardiff CF4 4XW, UK.

Letters should be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters above. The degrees and diplomas of each author must be given in a covering letter which must be signed personally by all the authors.

Correspondence presented in any other style or format may be the subject to considerable delay and may be returned to the author for revision.

The editors regret that failure to comply with the above requirements may result in a delay in publication of accepted papers.

REVIEW JOURNALS

This journal is covered by *Current Contents*, *ASCA* and the *Science Citation Index*.

Contents: Anaesthesia, vol. 41, no. 5, May 1986

EDITORIAL

C. Langton Hewer, MB, BS, FFARCS, MRCP, DA
T.B. Boulton 469

ORIGINAL ARTICLES

Single breath induction of anaesthesia, using a vital capacity breath of halothane, nitrous oxide and oxygen
N.C.T. Wilton and V.L. Thomas 472
Alfentanil supplemented anaesthesia for short procedures. A double-blind study of alfentanil used with etomidate and enflurane for day cases
R.I.W. Collin, G.B. Drummond and A.A. Spence 477
Sensitivity to propofol in the elderly
J.W. Dundee, F.P. Robinson, J.S.C. McCollum and C.C. Patterson 482
Premedication with cimetidine and metoclopramide. Effect on the risk factors of acid aspiration
S.K. Pandit, S.P. Kothary, U.A. Pandit and R.K. Mirakhur 486
Comparison of effects of fentanyl and alfentanil on intra-ocular pressure. A double-blind controlled trial
S.M. Mostafa, A. Lockhart, D. Kumar and M. Bayoumi 493
Caudal analgesia for perianal surgery. A comparison between bupivacaine and diamorphine
P.M. Bailey and S. Sangwan 499
Influence of ketanserin pretreatment on the haemodynamic responses to sternotomy
J.N. Cashman, M.A. Thompson and A. Bennett 505

CASE REPORT

Ventricular volume and ejection fraction in the diagnosis of the aetiology of low cardiac output in burned patients
J.A.J. Martyn, K. McKusick, H.W. Strauss and J.F. Burke 511

APPARATUS

A portable oxygen generator
L.W. Hall, R.E.B. Kellagher and K.J. Fleet 516
Selective bronchial intubation for one lung anaesthesia in thoracic surgery. A new method
S. Nazari, R. Trazzi, F. Moncalvo, A. Zonta and M. Campani 519
A comparison of five heat and moisture exchangers
M. Shelly, D. W. Bethune and R.D. Latimer 527

FORUM

Anaesthetic management and postoperative care of cardiac surgical patients in a general recovery ward
C. Aps, J.A. Hutter and B.T. Williams 533
Morbidity after day case laparoscopy. A comparison of two techniques of tracheal anaesthesia
M. Skacel, P. Sengupta and O.M. Plantevin 537
Bromazepam as oral premedication. A comparison with lorazepam
R. Ponnudurai and J. Hurdley 541
Fire in the operating theatre. Evacuation pre-planning may save lives
M.A. Moxon and M.E. Ward 543

CORRESPONDENCE 547

BOOK REVIEWS 562

ANAESTHETIC LITERATURE 568

SAFETY INFORMATION BULLETIN 574

STOP PRESS 574

Printed in Great Britain by Fletcher & Son Ltd, Norwich

Acc.
25.9.87

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain & Ireland

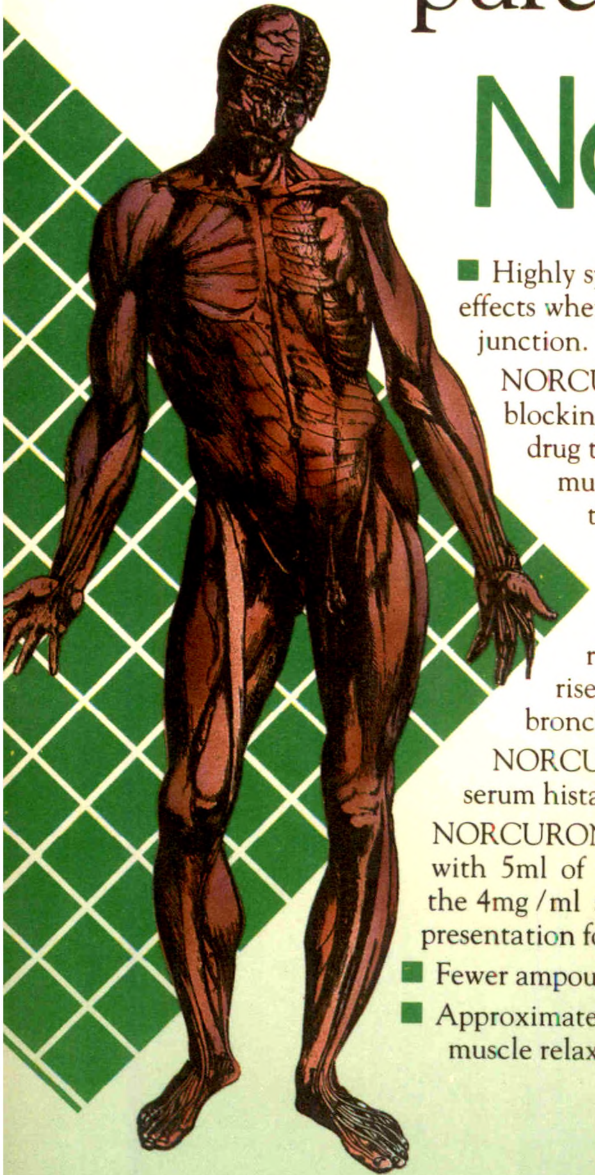
Volume 41 Number 6 June 1986

LIBRARY

Published for
The Association of Anaesthetists of Great Britain and Ireland by
Academic Press Grune & Stratton
London Orlando San Diego New York Austin
Boston Sydney Tokyo Toronto

ISSN 0003-2409

Muscle relaxation, pure and simple



NORCURON®

vecuronium bromide

- Highly specific – Muscle relaxants cause cardiovascular effects when their action is not specific for the neuromuscular junction.

NORCURON "... is the most specific neuromuscular blocking agent that has ever been synthesized. It is the drug that has by far the fewest side effects of any neuromuscular blocker. As a result it has the highest therapeutic ratio ... A dose can be selected that will give either short or long term duration of action."[1]

- Histamine release unlikely – Some muscle relaxants cause histamine release. This may give rise to such side effects as hypotension and bronchospasm.

NORCURON "... at 3.5 times the ED_{95} does not alter serum histamine levels."[2]

NORCURON is now available in a 10mg injection top vial with 5ml of water for injection as solvent. This replaces the 4mg/ml ampoule, the result being a more convenient presentation for the anaesthetist.

- Fewer ampoules to open.
- Approximately equipotent volume for volume with other muscle relaxants i.e. Pavulon.

ORCURON Muscle relaxation, pure and simple

10mg/vial presentation

Organon Teknika Limited

Cambridge Science Park, Milton Road,
Cambridge CB4 4FL

ldman SA; Clinical Experiences with Norcuron, Excerpta Medica (1983) 199-200
sta SA; Clinical Experiences with Norcuron, Excerpta Medica (1983) 183-184

ribing Information: Norcuron vials of 10mg vecuronium bromide with 5ml ampoule water for injection. **Uses:** non-depolarising neuromuscular blocking agent of short to medium duration. **Dosage:** Intravenous initial 0.08 10mg/kg incremental 0.03 to 0.05mg/kg. **Contraindications:** none known. Since there is no experience with the use of Norcuron in pregnant women, it cannot be recommended during pregnancy. Clinical studies show that uron can be used in childbirth by Caesarian section without effect on the newly born child. **Precautions and warnings:** In renal insufficiency a slight prolongation of neuromuscular block can be expected. Use very small , and extreme caution in myasthenia gravis or myasthenic syndrome unless prolonged post-operative respiratory assistance is intended. Dose carefully in myopathy, severe obesity, electrolyte disturbances, altered pH and after myelitis or dehydration. Neuromuscular blockade can be reversed with adequate doses of neostigmine together with atropine. **Interaction:** it is dangerous to give depolarising drugs (e.g. suxamethonium chloride) following a depolarising drug (e.g. Norcuron). Alkylating drugs (nitrogen mustards) may be a hazard in anaesthesia involving muscle relaxants. Anaesthetics, other drugs and the condition of the patient, may affect the magnitude and ration of action of **Norcuron** – see Data Sheet. **Side-effects:** none during clinical testing. **Overdosage:** use standard reversal agents, e.g. neostigmine or pyridostigmine. **Packs:** 20 vials 10mg **Norcuron,** 20 ampoules 5ml water jection. PL: 3524/0013.

Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

Editorial Board
Editor J. N. LUNN
Assistant Editors M. MORGAN, C. E. BLOGG, R. GREENBAUM, R. M. JONES
Chairman P. J. HELLIWELL
Advisory Editors R. S. ATKINSON, T. B. BOULTON
Members C. F. SCURR, P. J. F. BASKETT, D. J. HATCH and a representative of the Junior Anaesthetists Group
Ex officio
The President of the Association T. B. BOULTON
The Honorary Treasurer of the Association M. M. BURROWS
The Honorary Secretary of the Association M. T. INMAN
The Assistant Honorary Secretary of the Association P. MORRIS

Sub-editors of special sections
L. KAUFMAN Anaesthetic literature
A. PADFIELD National and local events
G. D. PARBROOK Audiovisual reviews
M. J. HARRISON Computer programs
JACQUELINE WELCH, DIANE WINTERBURN Reference librarians
D. V. BATEMAN Honorary proof reader

Address for literary contributions Dr J. N. Lunn, The Editor, *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK [telephone Cardiff (0222) 763601; Ansafone available].

Neither the Editor nor the Association of Anaesthetists of Great Britain and Ireland is in any way responsible for the statements made or the views expressed by contributors.

Investigations performed on man must conform to appropriate ethical standards including voluntary consent and acceptance by an ethical committee.

Published monthly (January–December) at 24–28 Oval Road, London NW1 7DX, England by Academic Press Inc. (London) Limited for the Association of Anaesthetists of Great Britain and Ireland, Rooms 475–478, Tavistock House South, Tavistock Square, London WC1H 9LG. As from December 2nd 1985, 9 Bedford Square, London WC1B 3RA.

1986, Volume 41, 12 issues. Inland £80.00 inclusive of postage and packing; abroad, $189.00 inclusive of postage and packing. Subscription orders should be sent to Academic Press Inc. (London) Limited, High Street, Foots Cray, Sidcup, Kent DA14 5HP (Tel. 01–300–0155). Send notices of change of address to the office of the Publishers at least 6–8 weeks in advance. Please include both old and new addresses.

Application to pay at second class postage rates pending at Jamaica, New York 11431, U.S.A.
Air freight and mailing in the U.S.A. by Publications Expediting Inc., 200 Meacham Avenue, Elmont, NY 11003, U.S.A.

© 1986 The Association of Anaesthetists of Great Britain and Ireland. The appearance of the code at the bottom of the first page of a paper in this journal indicates the copyright owner's consent that copies of the paper may be made for personal or internal use, or for the personal or internal use of specific clients in the U.S.A. This consent is given on the condition, within the U.S.A., that the copier pay the stated per-copy fee through the Copyright Clearance center Inc., 27 Congress Street, Salem, MA 01970, U.S.A. for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, for resale or for copying or distributing copies outside the U.S.A.

ISSN 0003–2409

Pocket Spirometer

- ☐ **INEXPENSIVE**
- ☐ **ACCURATE**
- ☐ **PORTABLE**
- ☐ **PEAK FLOW**
- ☐ **FEV$_1$**
- ☐ **FVC**

Now Available with Printer Output for Hardcopy of Data and Volume Time Curve using the new Micro Medical Instruments Pocket Printer.

The Unique *Hand Held* Spirometer

For more information on the Micro Medical Instruments Pocket Spirometer and our other respiratory products contact:-

Micro Medical Instruments

Micro Medical Instruments,
P.O. Box 6, Rochester, Kent.
ME1 2AZ, ENGLAND.
Telephone: Medway (0634) 712290

Joint Anaesthesiology Update

One day Anglo-American Symposium

Day Case Anaesthesia

Post-operative Analgesia

Chairmen:

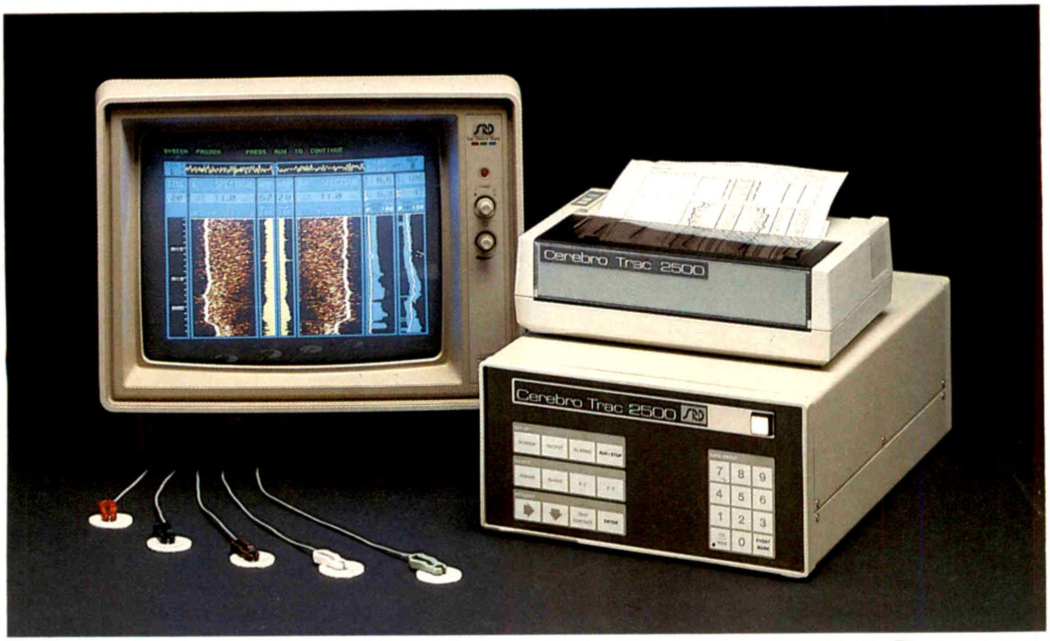
John T. Herbert, MD
Medical Director of Ambulatory Surgery and attending Anesthesiologist, Manhattan Eye, Ear & Throat Hospital, New York.

Michael Harmer, FFARCS
Consultant Anaesthetist, University Hospital of Wales, Cardiff.

London, 17th September, 1986

Information from:
Anglo-American Symposium Secretary, c/o Department of Anaesthetics, University Hospital of Wales, Cardiff, CF4 4XW.

CEREBRO-TRAC 2500



FULL CEREBRAL STATUS AT A GLANCE

CEREBRO-TRAC's unique, easy-to-read display format presents you with a trended Density Spectral Array from 2 channels of EEG, plus up to 4 related physiological parameters, on a single VDU screen.

This integrated at-a-glance display gives you the complete picture (real-time status and trends) ensuring rapid alert and response to early signs of cerebral hypoxia, ischemia and changes in anaesthetic depth.

The last word in cerebral monitoring, CEREBRO-TRAC is fully compatible with your existing monitoring equipment and designed to keep pace with future developments.

- Depth of Anaesthesia Monitoring
- Vascular and Cardiac Surgery
- Critical Care Monitoring

All this in a single integrated display:

- Real-Time EEG Waveforms
- Trended Density Spectral Array of FFT Processed EEG.
- Trended Display of Spectral Edge Frequency
- Trended EEG Amplitude
- Trended Display of Frontalis Muscle Activity
- Trended Displays of 4 other user-selected Parameters (Heart Rate, Blood Pressure, CO_2, O_2, Temperature etc.)
- Alarms and Event Markers

PLUS digital real-time values of all the above displayed parameters

Contact us now for a demonstration

NEUROSCIENCE LTD NEURO HOUSE, 1 ST JAMES ROAD, BRENTWOOD, ESSEX, ENGLAND. TELEPHONE: 0277 230909

In the USA: Neuroscience Inc., 210 Topaz Street, Milpitas, CA. 95035, USA.

European Journal of Anaesthesiology

Journal Editors
M.D. Vickers *Cardiff*
E. Nilsson *Lund*

Deputy Editor
P. Foëx *Oxford*

Editor of Commissioned Articles
C. Prys-Roberts *Bristol*

Assistant Editors
J.M. Desmonts *Paris*
T.E.J. Healy *Manchester*
W.R. MacRae *Edinburgh*
J. Tarnow *Berlin*

Advisory Editorial Board
H. Bergmann *Linz*
J.B. Brückner *Berlin*
S. Couremenos *Athens*
J.F. Crul *Nijmegen*
J.M. Desmonts *Paris*
W. Dick *Mainz*
W. Jurczyk *Poznan*
J. Lassner *Paris*
C. Manni *Rome*
M.A. Nalda-Felipe *Barcelona*
O. Norlander *Stockholm*
J.C. Otteni *Strasbourg*
C. Prys-Roberts *Bristol*
M. Rosen *Cardiff*
K. Steinbereithner *Vienna*
M.K. Sykes *Oxford*
T. Tammisto *Helsinki*
M.D. Vickers *Cardiff*
K.H. Weis *Würzburg*
J.S.M. Zorab *Bristol*

The *European Journal of Anaesthesiology*, the official publication of the European Academy of Anaesthesiology, publishes original work of high scientific quality. Preference is given to experimental work or clinical observation in man, and to laboratory work of clinical relevance. Each issue contains a commissioned review by an authority in a field of interest to those working in anaesthesiology or intensive care. Abstracts of Academy meetings, editorials, book reviews, news and notices are also included.

Subscription Information

European Journal of Anaesthesiology is published bi-monthly. Subscription rates for 1986 are £56.00 (UK and overseas). Subscription details for North America are available from Year Book Medical Publishers, 35 East Wacker Drive, Chicago, Illinois 60601, USA.

Order Form

Please tick the appropriate box and return to **Blackwell Scientific Publications Ltd, P.O. Box 88, Oxford, England.**

☐ I would like to subscribe to *European Journal of Anaesthesiology*
☐ I wish to pay by cheque/money order *(delete as necessary)* and enclose the sum of ....
☐ I wish to pay by Access/Barclaycard/VISA/Mastercard *(delete as necessary)*
Please debit my credit card no. ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐
Expiry date.......................... with the sum of ....
Signature.. Date ....
☐ Please send me a specimen copy of *European Journal of Anaesthesiology*

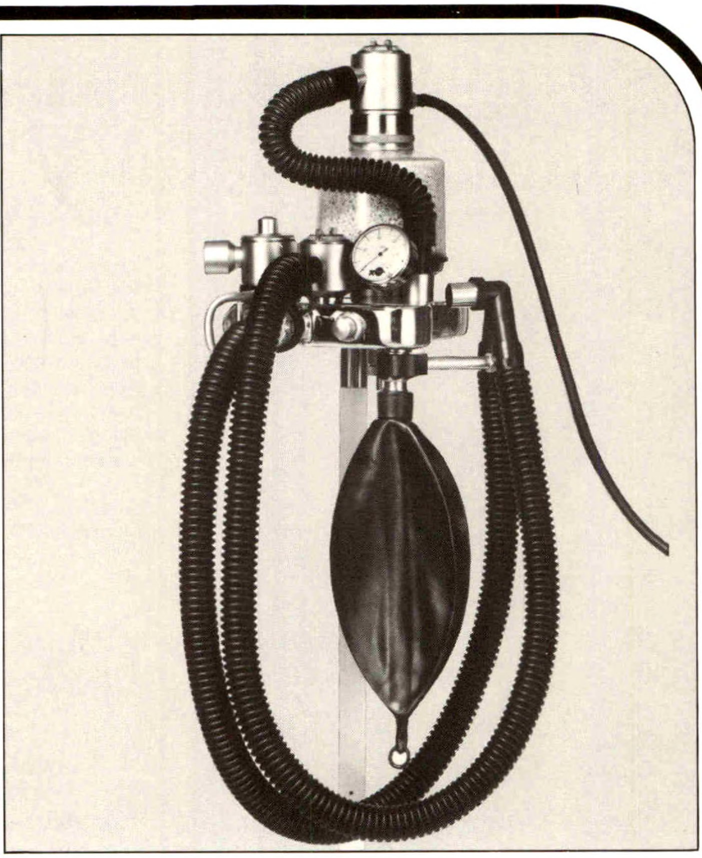
Name ....

Address ....

....

Blackwell Scientific Publications
P.O. Box 88, Oxford, England

A New Concept in Anaesthesia



The Ruben Circle

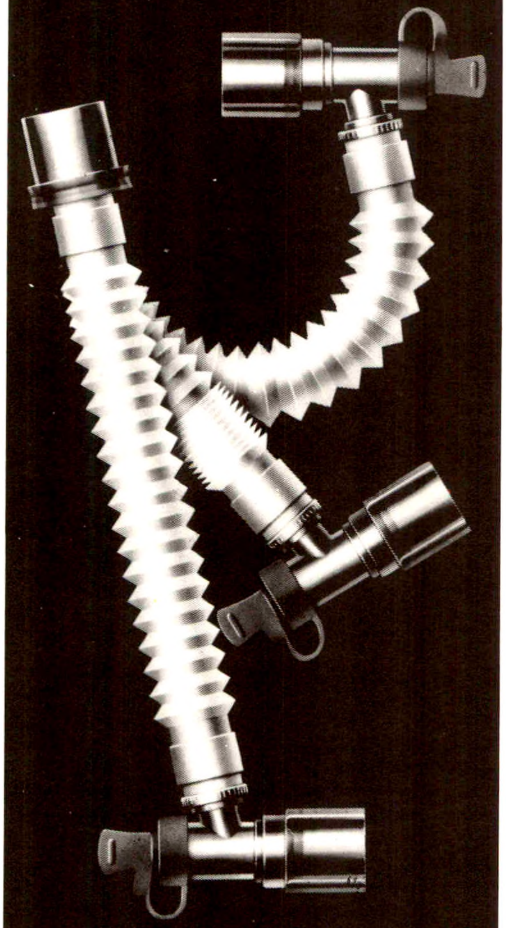
An anaesthesia system which is both open and closed at the same time.

- No spill valve adjustments
- No adjustment when changing between spontaneous controlled and assisted ventilation
- Fresh gas consumption extremely low
- No risk of pressure build-up
- Pollution risk eliminated
- Conforms to ISO standards

Ambu®

Ambu International · Søndre Ringvej 49 · DK-2600 Glostrup-Copenhagen · Denmark
Ambu International U.K. Ltd, Charlton Road, Midsomer Norton, BATH BA3 4DR. Telephone: (0761 416868)

SUPERSET™
CATHETER MOUNT



For the most mobile patient to ventilator circuit connection.

Seeing is believing—
Send for product sample:

Intersurgical®

Crane House, Gould Road, Twickenham,
Middlesex TW2 6RS, England
Telephone 01 - 755 1477 Telex: 8953147 INTERS G.

ANESTHESIA AND THE GERIATRIC PATIENT

Edited by
SUSAN WILSON KRECHEL, M.D.

Anesthesia and the Geriatric Patient represents the state of the art in the long-neglected area of anesthetic management of elderly patients. This new book features a collection of the most pertinent and informative topics on the subject. Approximately one-third of the book is devoted to basic science topics on physiology and pharmocology of aging as related to anesthesia practice with the remainder focusing on clinical aspects.

July 1984, 272pp., $42.50/£35.00
ISBN: 0.8089.1661.0/Order Code 792385

CLINICAL FEATURES IN ANESTHESIOLOGY

Edited by
JONATHAN L. BENUMOF,
University of California,
San Diego School of Medicine.

A Volume in the ANESTHESIA UPDATE Series

Covering the entire scope of anesthesia from both clinical and basic science perspectives, this comprehensive work presents the latest important developments in anesthesiology. With a concise emphasis on what is really "new" in the field, individual chapters by well-known experts discuss such vital issues as: • recent developments and breakthroughs in pharmocology • anesthesia techniques in operative, pre- and postoperative environments • special topics in the evolution of anesthesia, including a history of anesthesia and future directions • drug abuse in the medical profession.

1983, 288pp., $34,50/£29.00
ISBN: 0.8089.1580.0/Order Code 790548

Grune and Stratton

ORLANDO, FLORIDA 32887, U.S.A.
24-28 Oval Road, London NW1 7DX, England

A PRACTICE OF ANAESTHESIA FOR INFANTS AND CHILDREN

John F. Ryan
Associate Professor of Anaesthesia
Harvard Medical School, Anaesthetist
Massachusetts General Hospital
Charles J. Cote
Assistant Professor of Anaesthesia
Harvard Medical School, Associate Anaesthetist
Masschusetts General Hospital
L. David Todres
Associate Professor of Anaesthesia (Paediatrics)
Harvard Medical School
Anaesthetist & Paediatrician
Massachusetts General Hospital
Nishan Goudsouzian
Associate Professor of Anaesthesia
Harvard Medical School, Associate Anaesthetist
Massachusetts General Hospital
1985, 352pp., ISBN: 0.8089.1732.3
$67.50/£58.50 (UK only)

A Practice of Anaesthesia for Infants and Children is a ready reference for the practical management of anaesthesia for paediatric patients. The text is a distillation of the expertise of the paediatric anaesthesia team at Massachusetts General Hospital. It provides more than the limited direction of a manual by emphasising the principles and psychology upon which the practice is supported.

The book commences with the authors' philosophy of practice, followed by an overview of relevant developmental physiology. Preoperative evaluation is approached with special emphasis on medical and psychological problems. Specialised areas, such as cardiac and neuroanaesthesia, have been treated separately in this authoritative text, while subjects including malignant hyperthermia, regional anaesthesia and post-operative recovery care are approached in a practical manner. Illustrations, figures and tables complement the text; in particular the procedure section which pictorially details invasive techniques.

MUSCLE RELAXANTS:
Basic Clinical Aspects
Edited by Ronald M. Katz
October 1985, 320pp., ISBN: 0.8089.1784.6
$24.50/£20.50 (UK only)

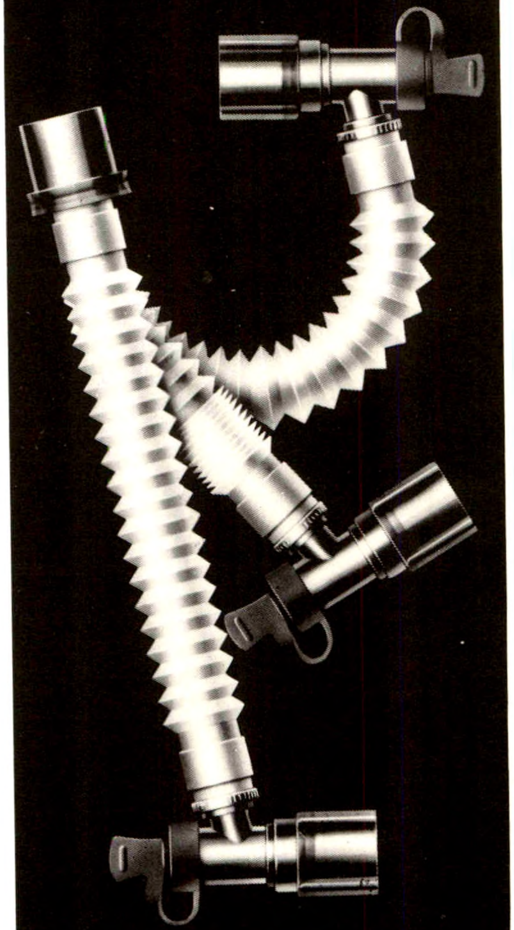
This new pocket-sized guide provides a quick and thorough reference to the clinical uses of muscle relaxants.

Its timely coverage includes the physiology and pharmacology of neuromuscular transmission, and the clinical use of such muscle relaxants as atracurium and vecuronium. Muscle relaxant antagonists, complications and controversies are discussed in detail. The use of muscle relaxants in patients with heart disease, renal failure and children are also included.

Prices are subject to change without notice

Grune & Stratton
24-28 OVAL ROAD, LONDON NW1 7DX
ORLANDO, FLORIDA 32887, USA

SUPERSET™
CATHETER MOUNT



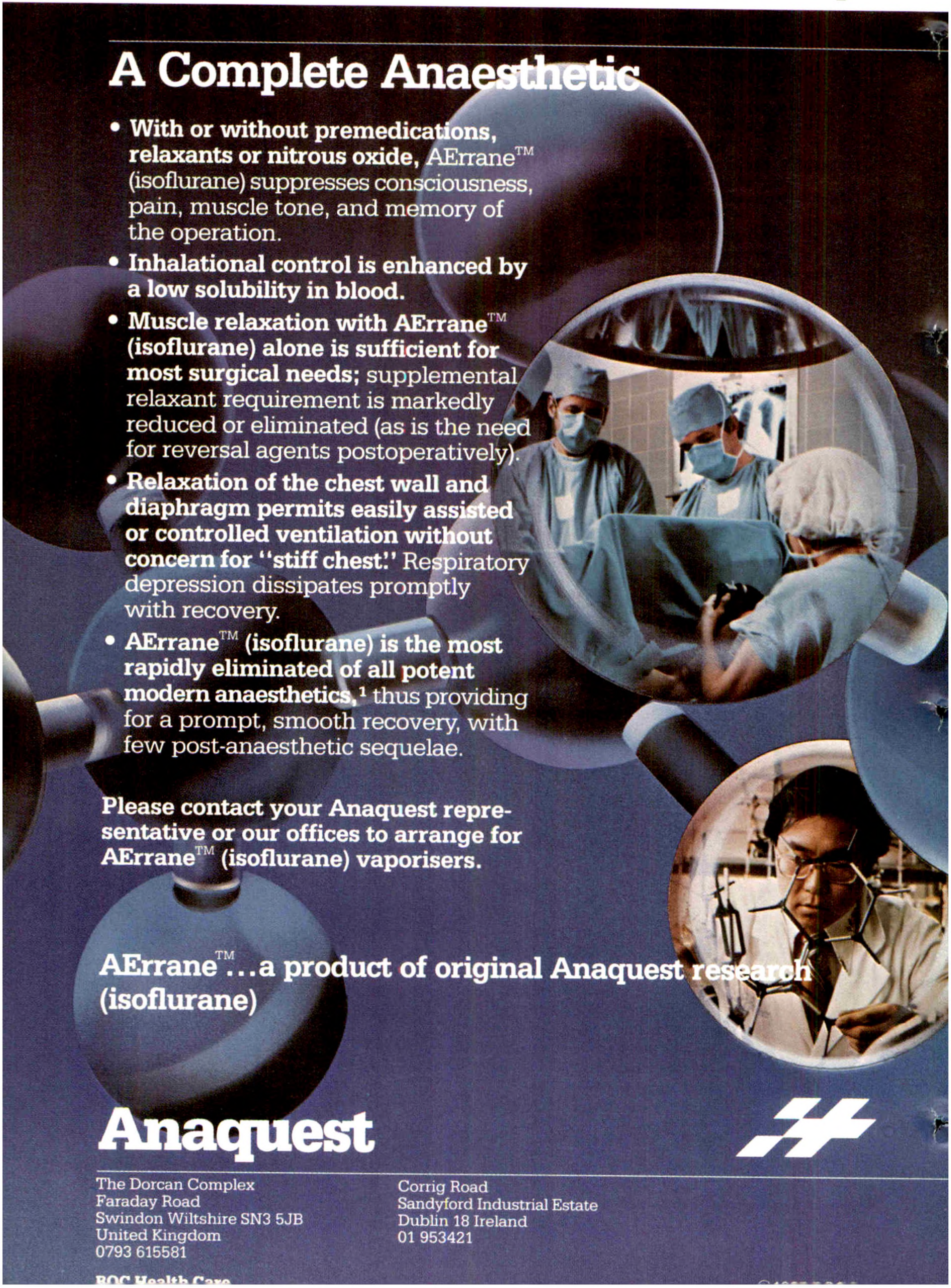
For the most mobile patient to ventilator circuit connection.

Seeing is believing—
Send for product sample:

Intersurgical®

Crane House, Gould Road, Twickenham,
Middlesex TW2 6RS, England
Telephone 01 - 755 1477 Telex 8953147 INTERS G.

AErrane™ (isoflurane)



A Complete Anaesthetic

- **With or without premedications, relaxants or nitrous oxide,** AErrane™ (isoflurane) suppresses consciousness, pain, muscle tone, and memory of the operation.
- **Inhalational control is enhanced by a low solubility in blood.**
- **Muscle relaxation with AErrane™ (isoflurane) alone is sufficient for most surgical needs;** supplemental relaxant requirement is markedly reduced or eliminated (as is the need for reversal agents postoperatively).
- **Relaxation of the chest wall and diaphragm permits easily assisted or controlled ventilation without concern for "stiff chest."** Respiratory depression dissipates promptly with recovery.
- **AErrane™ (isoflurane) is the most rapidly eliminated of all potent modern anaesthetics,[1]** thus providing for a prompt, smooth recovery, with few post-anaesthetic sequelae.

Please contact your Anaquest representative or our offices to arrange for AErrane™ (isoflurane) vaporisers.

AErrane™...a product of original Anaquest research (isoflurane)

Anaquest

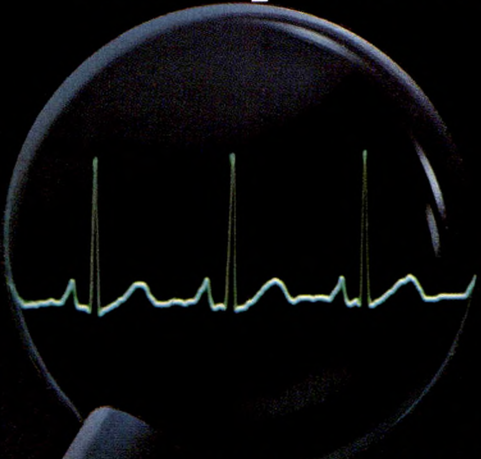
The Dorcan Complex
Faraday Road
Swindon Wiltshire SN3 5JB
United Kingdom
0793 615581

Corrig Road
Sandyford Industrial Estate
Dublin 18 Ireland
01 953421

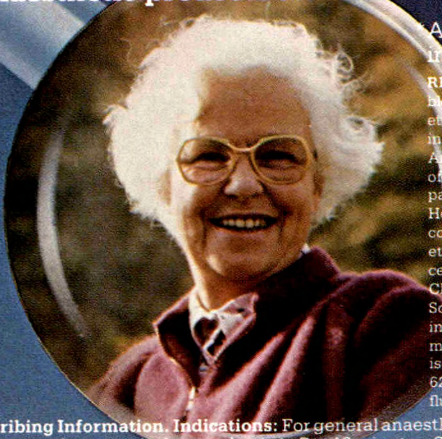
BOC Health Care

For the Sum of Your Patient's Anaesthetic Needs

Intraoperative Margins of Safety



- **AErrane™ (isoflurane) causes a dose-related decrease in peripheral resistance (and cardiac afterload) but little or no depression of myocardial function or cardiac output** (at normal levels of surgical anaesthesia, 1 to 1.5 MAC).[2] These effects are potentially useful in the elderly;[3] in patients with coronary artery disease,[4] and for induced hypotension in cerebral aneurysm surgery.[5]
- **Cardiac rhythm tends to remain stable.** A report from a large multicentre study of 6,798 patients states, "In none of the extensive analyses did isoflurane itself appear to be a factor associated with development of arrhythmias."[6] AErrane™ (isoflurane) also does not increase myocardial sensitivity to adrenalin[7] used for haemostasis or to endogenous catecholamines.[8]
- **An excellent choice for neurosurgery,** AErrane™ (isoflurane) causes no increase in intracranial pressure (ICP) when $PaCO_2$ is controlled at 25-30 mmHg.[9] ICP is readily lowered at any time by decreasing $PaCO_2$ (convulsive activity is not seen at any $PaCO_2$ level or anaesthetic concentration).
- **AErrane™ (isoflurane) is the least metabolized of all potent anaesthetics.**
- **AErrane™ (isoflurane) has been used in more than 20 million anaesthetic prodecures.***



*AErrane™ (isoflurane) is not approved for use in obstetrics.

REFERENCES: 1. Cromwell TH, et al: Forane uptake, excretion and blood solubility in man. Anesthesiology 35:401-408, 1971. 2. Stevens WC et al: The cardiovascular effects of a new inhalation anesthetic, Forane in human volunteers at constant arterial carbon dioxide tension. Anesthesiology 35:8-16, 1971. 3. Linde HW, et al: Cardiovascular effect of isoflurane and halothane during controlled ventilation in older patients. Anesth Analg 54:701-704, 1975. 4. Mallow JE, et al: Hemodynamic effects of isoflurane and halothane in patients with coronary artery disease. Anesth Analg 55:135-138, 1976. 5. Lam AM, et al: Cardiovascular effects of isoflurane-induced hypotension for cerebral aneurysm surgery. Anesth Analg 62:742-748, 1983. 6. Levy W Clinical evaluation of isoflurane: Cardiac arrhythmias. Can Anaesth Soc J 29 (suppl): 828-834, 1982. 7. Johnston RR, et al: A comparative interaction of epinephrine with enflurane, isoflurane and halothane i man. Anesth Analg 55:709-712, 1976. 8. Suzukawa M, et al: Use of isoflurane during resection of pheochromocytoma. Anesth Analg 62:100-103, 1983. 9. Adams RW, et al: Isoflurane and cerebrospinal fluid pressure in neurosurgical patients. Anesthesiology 54:97-99, 1981

Prescribing Information. Indications: For general anaesthesia. **Dose:** Inspired concentrations of 1.5 to 3.0% AErrane produce surgical anaesthesia in 7 to 10 minutes. Surgical anaesthesia can be maintained with 1.0 to 2.5 AErrane when used concomitantly with nitrous oxide. **Contraindications:** Known sensitivity to AErrane halogenated anaesthetics; known or suspected genetic susceptibility to malignant hyperthermia. **Side F** Hypotension, respiratory depression, arrhythmias, elevated white blood count, shivering, nausea, vom have been reported. **Product Licence Number:** 5247/0002.

Acta Anaesthesiologica Scandinavica

Editor-in-Chief
JAN EKLUND,
Stockholm, Sweden.

Co-Editors
VIGGO DYRBERG,
Copenhagen, Denmark
PER H. ROSENBERG,
Helsinki, Finland

Associate Editors
MARTIN H: SON HOLMDAHL,
Uppsala, Sweden
ANTON HAUGE,
Oslo, Norway
OLAFUR JONSSON,
Reykjavik, Iceland
OLE SECHER,
Copenhagen, Denmark
TAPANI TAMMISTO,
Helsinki, Finland

Acta Anaesthesiologica Scandinavica publishes papers on original work in anaesthesiology and subjects related to its basic sciences, on condition that they are contributed exclusively to this journal. The journal is published in English.

Subscription
One volume of eight issues is published annually. Subscription Price 1986: D.kr. 750.00 (£58.50, DM 221.25) including postage. USA and Canada: US$ 91.00 including postage and air freight, payable in advance. Prices are subject to exchange-rate fluctuations. In addition to the normal 6 issues a number of supplements are delivered separately to subscribers free of charge.

ORDER FORM

Send to Munksgaard International Publishers Ltd.
35 Norre Sogade, DK-1370 Copenhagen K, Denmark
or
Munksgaard International Publishers Ltd.
c/o Publications Expediting Inc.
200 Meacham Avenue, Elmont, NY 11003, USA

☐ I would like to subscribe to Acta Anaesthesiologica Scandinavica from 1986 and I enclose my personal cheque for ____________

☐ Please send me a free specimen copy of Acta Anaesthesiologica Scandinavica.

Name: ______________________________

Address: ______________________________

____

Prescribing information

Indication Muscle relaxation for surgical and anaesthetic procedures. **Dosage** Response is variable, but as a guide: Adults: 0.20-0.25mg/kg intravenously for approximately 20-30 minutes' relaxation, 0.30mg/kg for approximately 40 minutes' relaxation. Children: 0.125 to 0.2mg/kg bodyweight. **Contra-indications** Hypersensitivity to alcuronium, myasthenia gravis; myasthenic (Eaton-Lambert) syndrome. **Precautions** Dosage requirements may be altered in renal impairment, hepatic and neuromuscular diseases, and by concomitant use of antibiotics of the polymixin and aminoglycoside groups, volatile anaesthetics, drugs with local anaesthetic properties, ganglion-blockers, electrolytes (Mg, Na, K, Ca). Avoid during pregnancy. **Side-effects** Hypotension and, less frequently, tachycardia. Some cases of anaphylactoid reaction have been recorded. **Presentation** Ampoules containing 10mg alcuronium chloride in 2ml packings of 10. **Basic NHS Cost** Alloferin ampoules 10mg x 10, £5.24. **Licence Number** 0031/5000

Alloferin is a trade mark.

Date of preparation April 1986.

In both short and prolonged surgery

A single dose of Alloferin (0.20-0.25mg/kg) provides muscle relaxation for approximately 20-30 minutes[2] and a 0.30mg/kg dose gives about 40 minutes of relaxation. The relaxation can be maintained for longer procedures with "no noticeable accumulation" of Alloferin[3] and the number of repeat doses required is similar to that with tubocurarine or pancuronium[4]

Considerable cardiovascular stability

Alloferin allows blood pressure and heart rate to be kept within acceptable limits in most patients due to lack of marked histamine-releasing, ganglion-blocking or vagolytic actions[2,5,6]

Easy reversal for uncomplicated recovery

Alloferin has been found to be easi to reverse with neostigmine than either pancuronium or tubocurarin

---

References 1. Brit.J.hosp.Med.,1980,*23*,153. 2. Ann.Chir.Gynaec.,1977,*66*,113. 3. Europ.J.clin. Pharmacol.,1980,*17*,449. 4. Anesth.Analg. curr.Res.,1971,*50*,926. 5. Int.Anesth.Clins,1979, *17*,13. 6. Brit.J.Pharmacol.,1980,*70*,501.

A useful
muscle-relaxant
for routine use[1]

ALLOFERI

ALCURO

ROCHE

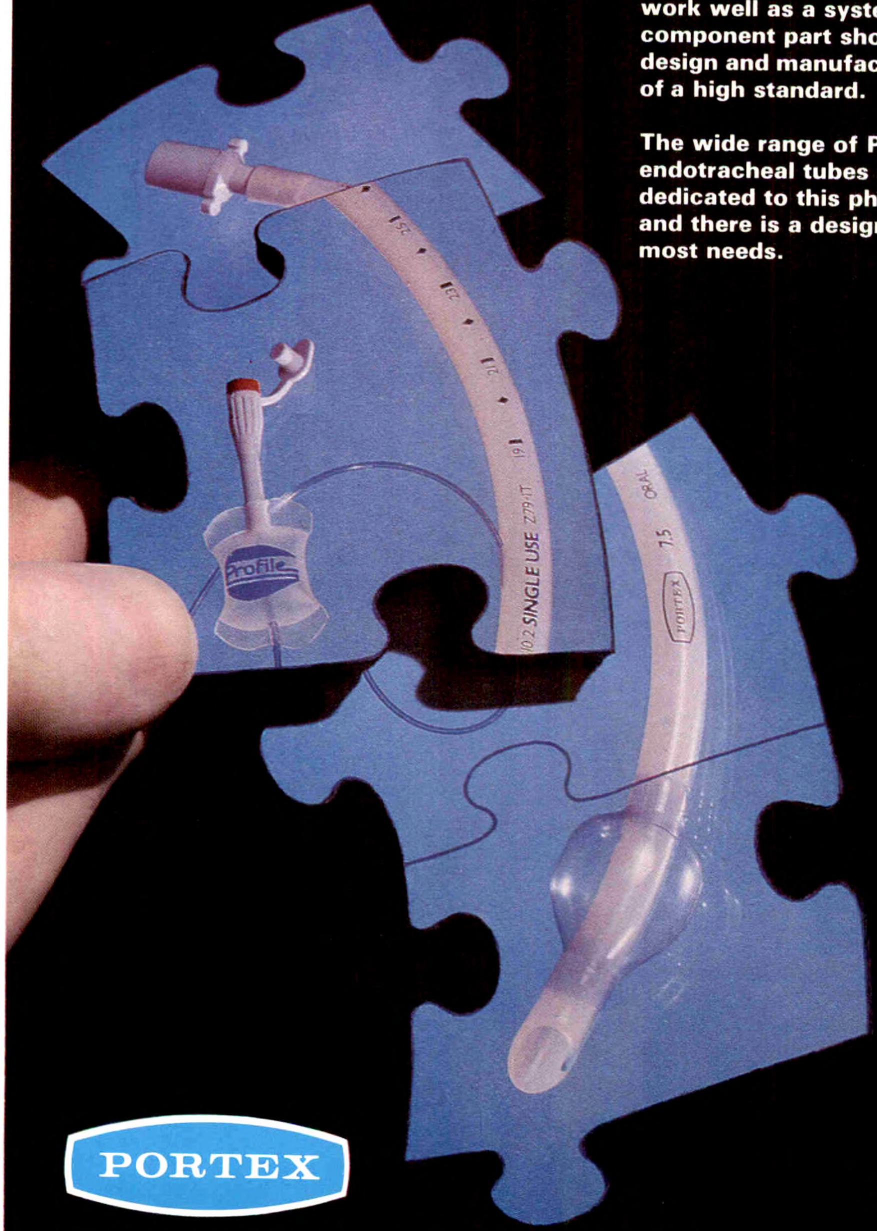
Roche Products Limited
PO Box 8 Welwyn Garden City
Hertfordshire AL7 3AY

J017030/486

EACH "PIECE" PLAYS ITS PART

For an endotracheal tube to work well as a system, each component part should by design and manufacture, be of a high standard.

The wide range of Portex endotracheal tubes are all dedicated to this philosophy and there is a design to suit most needs.



PORTEX

PORTEX LIMITED, Hythe, Kent, England, CT21 6JL.
Tel: Hythe (0303) 66863 & 60551. Telex: 96165. Facsimile: (0303) 66761.

sims A Smiths Industries Medical Systems Company

1984

Anaesthesia, 1986, Volume 41, pages 575–578

Editorial

Halothane hepatitis in children

The report of 'halothane hepatitis' in an 11-month-old child by Whitburn and Sumner (p. 611) encourages further debate on the direct cause and effect relationship between exposure to halothane (or other inhalational agents) and postoperative liver damage, and the relevance of the syndrome to modern anaesthetic practice. If, as suggested,[1] the elegant tests for circulating antibodies indeed prove to be specific pathognomonic evidence of halothane hepatitis, this report certainly provides the second valuable, well-documented warning that the syndrome *may* occur in children (the first was in 1982[2]). However, in some respects, the report raises several questions which increase further the apparent complexity of the whole problem.

Few would deny the probability that halothane hepatitis does occur rarely, that the syndrome is responsible for at least some of the reported cases of 'unexplained hepatitis following halothane' and that it remains the responsibility of the anaesthetist to minimise the risk, if possible. Some authorities believe that the metabolically related damage demonstrable in a variety of somewhat arcane animal models (of doubtful relevance to the syndrome in man), coupled with the minor alterations in liver function test results reported commonly following exposure to halothane, suggest that mild (subclinical) halothane hepatitis is, in fact, very common. This view is held despite the distinct possibility that such minor changes may equally well reflect the largely unavoidable alterations in hepatic blood flow and metabolism engendered by exposure to anaesthesia and surgery. However, clinically significant halothane hepatitis appears to be rare in adults and very rare indeed in children. Assessments of the overall incidence of halothane hepatitis vary widely, an inconsistency hardly surprising in view of the guesswork often applied both to the numerator (number of cases of halothane hepatitis) and the denominator (total number of halothane administrations). The incidence quoted by Whitburn and Sumner of between 1 in 6000 and 1 in 22 000 serves as a reasonable point of comparison. Wark[3] reviewed 165 400 computerised records of anaesthetics administered between 1957 and 1979 at The Hospital for Sick Children, Great Ormond Street and described two patients with otherwise inexplicable post-halothane hepatitis. This incidence of about 1 in 82 000 is certainly much lower than the range of incidences reported in adults. Furthermore, 267 patients received multiple halothane exposures within 28 days without obvious hepatic problems—this is a useful negative finding which confirms previous experience with most adults repeatedly exposed to halothane.

Why should the incidence of halothane hepatitis be so much lower in children? If the mechanism in man is indeed direct hepatotoxicity of intermediate metabolites of halothane, (*if* the animal model evidence can rationally be extrapolated to man), children, who are apparently capable of metabolism of halothane by reductive pathways (to a degree similar to that seen in adults[4]), should be similarly at risk. This view is further illustrated by the report by Haxholdt and her colleagues (p. 579) that even a single exposure to halothane in children results in hepatic microsomal enzyme induction comparable to that seen in adults. The suggestions that children may either have higher levels of hepatic free radical scavengers (despite the fact that the role of glutathione depletion in animal models is far from clear) or else have greater powers for hepatic recovery are attractive but await confirmation.[4]

On the other hand, the rarity of the clinical syndrome and the apparent irrelevance of dose-dependency suggest very strongly that metabolism alone is not responsible. The alternative hypothesis of hypersensitivity (either as a primary mechanism or following initial production of reactive intermediate metabolites capable of combining with protein to form antigenic complexes) similarly fails to explain the rarity of halothane hepatitis in children. Immune competence is apparently present from birth,[5] and the reported incidence of major adverse reactions to drugs of between 1 in 2500 and 1 in 10 000 children[6] suggests, once again, that adults and children should be similarly at risk. It is of interest

0003–2409/86/060575 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

that, in contrast to the frequent history of allergy among adults with halothane hepatitis, such a history does not seem to be a feature of reported cases in children. The child reported in this issue developed eosinophilia in association with the episode of postoperative hepatitis—a finding commonly reported in patients with halothane hepatitis and suggestive of an immunological response.

The cases reported here (p 611), and elsewhere,[2] raise several important points. Both children developed halothane hepatitis following several rapidly repeated exposures, but others seem to have followed single exposure.[3] It is quite clear that *ex cathedra* statements about the safe period between halothane exposures in *adults* do not withstand scientific scrutiny. The syndrome is associated with rapidly repeated exposures, however, and many authorities advocate not within a month (although this may be nothing more than a convenient period in our calendar which was first highlighted by analysis of reports to the Committee on Safety of Medicines.[7]) More recently, the term 'rapidly repeated' has been applied to 4–8 weeks or to 3 months, with such suggestions quite understandably serving perceived medicolegal requirements rather than being based on new important evidence. However, the modern anaesthetist is fortunate in having many alternative agents and techniques at his command. If such alternatives are considered to be as safe overall (in his hands) for a particular surgical procedure then, even if very recent halothane exposure was *not* followed by signs of possible adverse reaction (such as jaundice or, possibly, *late* pyrexia), he may be better advised to choose the alternative. This medicolegally sensitive advice applies despite knowledge of the innumerable multiple halothane anaesthetics administered without problems and despite the fact that the substitution of alternative agents for second and subsequent anaesthetics has by no means been shown conclusively to be better for patients (either hepatically or overall). In children, however, the position in even less clear (if that is possible!).

Should an apparent incidence of halothane hepatitis of 1 in 82 000 influence usage of halothane in a patient population in whom the agent has been proved to be of great value with regard to overall safety? With the obvious *caveat* regarding any patient who has exhibited jaundice, or (perhaps) *late* unexplained pyrexia following previous exposure to halothane, who should not, of course, be re-exposed to the drug, can one advocate the continued use of halothane (even rapid repetition) in children? A rational approach must be that halothane remains a very valuable agent in children (as indeed it does in adults). The problem must be viewed in perspective. If senior anaesthetic staff at one of the leading hospitals for sick children, while wisely alerting us to the possibility of halothane hepatitis in children and stressing the need to keep the possibility in mind, still regard the repeated use of halothane in children as safe anaesthetic practice, then, at present, that is good enough for the present author. That anaesthetists must best serve the overall interests of their patients may be exemplified by a recent timely comparison of halothane and isoflurane in unpremedicated children presenting for short outpatient procedures.[8] The authors report that the use of isoflurane was associated with more problems of coughing, excessive secretions and laryngospasm during induction and, similarly, more violence and upper respiratory tract problems during recovery. Such difficulties may, to some extent, reflect inexperience with a new agent, but it may be that halothane still reigns supreme in that particular environment at least.

What of unexplained hepatitis following exposure to enflurane or isoflurane? The relatively limited metabolism of enflurane (2 percent) and isoflurane (0.2 percent) compared with halothane (20 percent) suggests that, whether metabolism proves to be the sole mechanism for toxicity or merely a prerequisite for a subsequent immunological reaction, these newer agents might be expected to have less potential for hepatic damage. Some authors believe that the curtailment of halothane usage and the corresponding increase in the use of first enflurane and latterly isoflurane has been associated with a reduction in the numbers of reports of unexplained postoperative hepatitis. A recent review of reports of enflurane-associated hepatitis[9] includes one 15-year-old patient, although, just as in the case of halothane, the validity of some of those cases has, quite rightly, been questioned.[10] The only mention of a case associated with isoflurane appears, rather unconvincingly, as part of a report of isoflurane usage in Canada.[11] No doubt, isolated case reports will appear and their relevance will have to be judged on their merits. If at least some cases of unexplained hepatitis following exposure to anaesthesia and surgery prove to be coincidental non-A non-B viral hepatitis, sporadic cases associated with isoflurane must surely surface as usage of the agent becomes widespread.

Whitburn and Sumner clearly recognise that viral infection remains an important possible alternative diagnosis in any patient with postoperative hepatitis, although in their patient markers for hepatitis A and B were absent and specific tests for circulating antibodies were positive. It remains true that viral hepatitis cannot yet be excluded in any patient with absolute certainty. It is of interest that, of children suffering acute hepatitis severe enough to warrant hospital admission, 5 percent have non-A non-B infection,[12] for which there is, at present, no marker. Furthermore, despite some claims to the contrary, viral and halothane hepatitis remain virtually indistinguishable biochemically, clinically and histologically. It remains possible that non-A non-B hepatitis might be responsible for, say, those cases of halothane hepatitis following single exposure, or for the syndrome in those anomalous patients who receive several rapidly repeated exposures to halothane uneventfully and then develop hepatitis after one further exposure years later.[13] Such anomalies are equally difficult to explain on either toxicity or hypersensitivity grounds.

In the report by Whitburn and Sumner, subsequent anaesthesia, using a halothane-free machine, was followed by low grade pyrexia and eosinophilia. The child did not develop jaundice, but it is unfortunate that pre- and postoperative liver function test results were not reported. The use of a halothane-free machine in patients previously suffering possible halothane hepatitis is obviously intellectually satisfying, but based on no evidence whatsoever. A policy of extreme caution and attention to detail dictates that a virgin machine might afford maximal protection to such a patient. However, the present author has seen 19 patients with apparent halothane hepatitis subsequently anaesthetised on halothane-contaminated machines without ostensible hepatic problems. One can argue that such an outcome favours the hepatotoxicity theory, inasmuch as the very small contaminating dose of halothane to which these patients were undoubtedly exposed was insufficient to result in toxic levels of intermediate metabolites. On the other hand, one might argue that such a small dose would not result in sufficient antigen to trigger an immunological response. Of course, had Whitburn and Sumner not been quite so fastidious and used a standard machine, the low grade pyrexia and eosinophilia might have been attributed for evermore to the rather unwise exposure of a sensitive patient to a very low dose of the offending drug. As it stands, the postoperative changes remain quite unexplained—as do so many aspects of this fascinating topic.

One burning question urgently needs answering from the medicological point of view. With regard to the advisability of repeated exposures to halothane, at what age does an older child become a young adult?

The London Hospital,
Whitechapel,
London, E1 1BB

B. WALTON

References

1. NEUBERGER J, GIMSON AES, DAVIS M, WILLIAMS R. Specific serological markers in the diagnosis of fulminant hepatic failure associated with halothane anaesthesia. *British Journal of Anaesthesia* 1983; **55:** 15–9.
2. LEWIS RB, BLAIR M. Halothane hepatitis in a young child. *British Journal of Anaesthesia* 1982; **54:** 349–54.
3. WARK HJ. Postoperative jaundice in children. The influence of halothane. *Anaesthesia* 1983; **38:** 237–42.
4. PLUMMER JL, VAN DER WALT JH, COUSINS MJ. Reductive metabolism of halothane in children. *Anaesthesia and Intensive Care* 1984; **12:** 293–5.
5. BAREN F, GOUDEAU A, DENIS F, YVONNET B, CHIRON JP, COURSAGET P, DIOP MAR I. Immune response in neonates to hepatitis B vaccine. *Lancet* 1982; **1:** 251–3.
6. KUZEMKO JA. In FORFAR JO, ARNEIL GC (eds). *Textbook of paediatrics*, 3rd Edn. Edinburgh: Churchill Livingstone, 1984; **2:** 1743.
7. INMAN WHW, MUSHIN WW. Jaundice after repeated exposure to halothane: a further analysis of reports to the Committee on Safety of Medicines. *British Medical Journal* 1978; **2:** 1455–6.
8. PANDIT UA, STEUDE GM, LEACH AB. Induction and recovery characteristics of isoflurane and halothane anaesthesia for short outpatient operations in children. *Anaesthesia* 1985; **40:** 1226–30.
9. LEWIS JH, ZIMMERMAN HJ, ISHAK KG, MULLICK FG. Enflurane hepatotoxicity. A clinicopathological study of 24 cases. *Annals of Internal Medicine* 1983; **98:** 984–92.
10. DYKES MHM. Is enflurane hepatotoxic? *Anesthesiology* 1984; **61:** 235–7.

Anaesthesia, 1986, Volume 41, pages 579–581

Increased hepatic microsomal activity after halothane anaesthesia in children

OLGA ST. HAXHOLDT, S. LOFT, ANETTE CLEMMENSEN AND ELSE HJORTSØ

Summary

The effect of anaesthesia and surgery on microsomal enzyme activity was studied in 19 children aged 4–9 years, scheduled for tonsillectomy. The children were randomly allocated to either halothane or ketamine anaesthesia. Antipyrine clearance was measured before and 4 days after surgery by a salivary one-sample technique. Statistically significant ($p < 0.001$) increases in antipyrine clearance was found in children who received halothane anaesthesia. The antipyrine clearance was increased by a mean of 26% 4 days after surgery, compared with a pre-operative control measurement. No significant change in antipyrine clearance was observed in children who received ketamine anaesthesia. There was also a significant difference in antipyrine clearance changes after surgery between the two groups ($p < 0.05$). Halothane has enzyme-inducing properties after a single exposure in children, while a single dose of ketamine does not.

Key words

Anaesthetics, volatile; halothane.
Induction; enzymes.

Increased microsomal enzyme activity in adults has been shown after various operations with either general or regional anaesthesia.[1-3] This indicates that, in adults, surgery *per se*, regardless of type of anaesthesia employed, is responsible for the enzyme induction. The effect of surgery and anaesthesia on microsomal enzyme activity has not been studied in this context in children. We therefore investigated the effect, in children, of tonsillectomy under halothane and ketamine anaesthesia on microsomal enzyme activity assessed by antipyrine clearance in a prospective randomized study.

Material and methods

Nineteen children aged 4–9 years, scheduled for elective tonsillectomy, were investigated. Informed consent was obtained from the parents and the study was approved by the ethical committee of Copenhagen county. None of the children had any history of hepatic disease and none was taking any drugs at the time of the investigation.

All children were premedicated with rectal diazepam solution (0.75 mg/kg). The children were randomly assigned to receive either halothane anaesthesia (10 children) or ketamine anaesthesia (10 children). One child from the ketamine group was excluded owing to a missing sample. Halothane was administered in 70% nitrous oxide in oxygen via a facemask. The ketamine anaesthesia was induced by intramuscular injection of ketamine (Ketalar®)

Olga St. Haxholdt, MD, Senior Registrar, Department of Anaesthesia, S. Loft, MD, Research Fellow, Department of Medicine, Anette Clemmensen, Chief Nurse, ENT Department and Else Hjortsø, MD, Junior Registrar, Department of Anaesthesia, Gentofte Hospital, University of Copenhagen, Denmark.

0003–2409/86/060579 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

10 mg/kg and atropine 0.01 mg/kg. Tracheal intubation was facilitated by suxamethonium 1 mg/kg. For maintenance of the ketamine anaesthesia, nitrous oxide/oxygen was administered, supplemented by intravenous ketamine 1–2 mg/kg as required. In both groups, pethidine 0.5 mg/kg was administered intramuscularly, following induction of anaesthesia. After surgery, acetaminophen, which has been shown not to have enzyme inducing properties,[4] was administered rectally for pain relief.

The day before surgery, the fasting children ingested antipyrine 20 mg/kg dissolved in juice. Twenty-two to 24 hours later, saliva was collected. Four days after surgery, the antipyrine ingestion with saliva collection 22–24 hours later was repeated. Saliva samples were stored at −20°C until analysis by high pressure liquid chromatography.[5] One-sample antipyrine clearance (OSAC) was calculated as:

$$\text{OSAC} = \frac{\ln D/Vd\text{-}\ln Ct}{t}\, Vd$$

where D is the administered dose, Vd is the volume of distribution estimated from age and body weight and height and Ct is the saliva concentration of antipyrine at the sampling time t. Comparison within a group was done by paired t-test and between groups by unpaired t-test. All p-values less than 0.05 were considered statistically significant. The excellence of fit to the normal distribution of the postsurgery changes in antipyrine clearance was tested by the Kolmgorov-Smirnov method.

Results

The results are summarised in Table 1 and Fig. 1. Only in the group of children receiving halothane anaesthesia was there a statistically significant increase in the one-sample antipyrine clearance (OSAC) after surgery ($p<0.001$). The mean increase was 26%, but with a great interindividual variation, i.e. in one child the increase was 72%. All but one of the children in the ketamine group showed a slight increase in the postsurgery OSAC, but the increase was not significant.

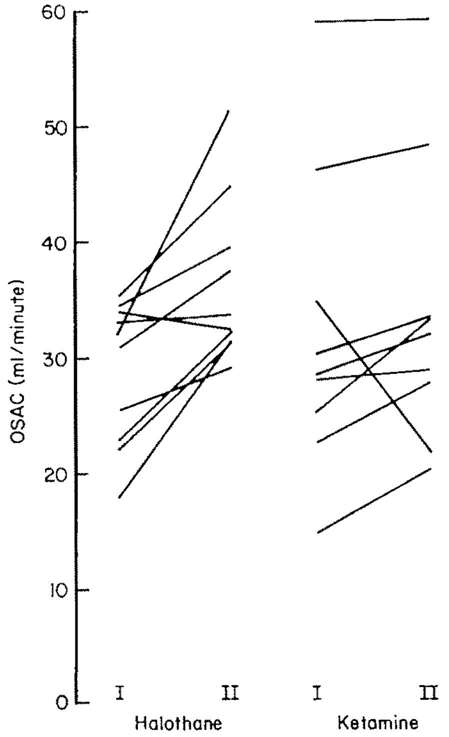


Fig. 1. OSAC (one-sample antipyrine clearance) before (I) and after (II) surgery and halothane or ketamine anaesthesia in children.

The two groups were comparable in regard to personal characteristics and duration of anaesthesia. However, the increase in OSAC in the

Table 1. Personal characteristics and one-sample antipyrine clearance (OSAC) before and after surgery under halothane or ketamine anaesthesia in 19 children

Anaesthesia	Weight (kg)	Height (cm)	Age (years)	Duration of anaesthesia (minutes)	OSAC presurgery (ml/minute)	OSAC postsurgery (ml/minute)	Δ OSAC (ml/minute)
Halothane $n = 10$	23 (2.8)	121.7 (6.2)	6.5 (1.4)	48 (5.6)	29.0 (5.8)	36.5 (6.7)	7.5 (5.8) ($p<0.001$)
Ketamine $n = 9$	25.8 (5.3)	126.4 (10.3)	6.7 (1.6)	53 (10)	32.3 (12.5)	34.1 (11.8)	1.7 (5.7) ($p>0.4$)
Halothane vs ketamine	ns	ns	ns	ns	ns	ns	($p<0.05$)

Values are given as mean (SD); ns = not significant.

halothane group was significantly higher than in the ketamine group ($p < 0.05$). The hypothesis of normal distribution of the changes in antipyrine clearance within each group as well as in the groups combined could not be rejected at the 20% level.

Discussion

The effect of surgery and anaesthesia on hepatic microsomal enzyme activity in children has not been studied previously. We investigated the effect of tonsillectomy under halothane or ketamine anaesthesia on antipyrine elimination, one of the most widely used indicators of microsomal enzyme activity.[4] Antipyrine clearance was measured from a single sample of saliva, which is as accurate as multiple samples and more acceptable to children.[5]

The main result of the study is a statistically significant increase in antipyrine clearance in children receiving halothane anaesthesia. The increase was of the same magnitude as previously reported in various studies in adults subjected to surgery of similar duration,[1-3] when the increase has been observed both after general and regional anaesthesia. This indicates that surgery *per se* is responsible. However, in the ketamine group in our study, no significant change in antipyrine clearance was observed.

The effect of surgery under ketamine anaesthesia on microsomal enzyme activity has not been investigated previously. Meanwhile, the animal experiments have shown that single doses of ketamine do not cause enzyme induction,[6] while repeated administration has enzyme-inducing effects.[6,7] None of the children investigated had recently been anaesthetised and none was taking any drugs. The surgical stimulus of tonsillectomy was obviously insufficient to induce enzyme activity, probably because the operation stress was of minor magnitude.[8] This indicates that halothane alone is able to induce microsomal enzyme activity, even under minor surgical stress.

Halothane has been shown to have an intrinsic enzyme-inducing property. Thus, occupational exposure to waste halothane leads to increased antipyrine clearance.[9] The average increase in antipyrine clearance in the present study was moderate (mean 26%), indicating only insignificant alterations in hepatic drug metabolism. However, the interindividual variation was great, as one child experienced an increase of 72%.

In conclusion, we have demonstrated that halothane leads to increased antipyrine clearance in children after a single exposure, even under conditions of minor surgical stress. On the other hand, ketamine does not have enzyme-inducing properties after single doses in children.

References

1. Duvaldestin P, Mazze RI, Nivoche Y, Desmonts JM. Enzyme induction following surgery with halothane and neurolept anaesthesia. *Anesthesia and Analgesia* 1981; **60:** 319–23.
2. Nimmo WS, Thompson PG, Prescott LF. Microsomal enzyme induction after halothane anaesthesia. *British Journal of Clinical Pharmacology* 1981; **12:** 433–4.
3. Loft S, Boel J, Kyst A, Rasmussen B, Hansen SH, Døssing M. Increased hepatic microsomal enzyme activity after surgery under halothane or spinal anesthesia. *Anesthesiology* 1985; **62:** 11–6.
4. Vesell ES. The antipyrine test in clinical pharmacology: conceptions and misconceptions. *Clinical Pharmacology and Therapeutics* 1979; **26:** 275–86.
5. Loft S, Haxholdt O, Døssing M. Antipyrine clearance in children from single saliva samples. *British Journal of Clinical Pharmacology* 1985; **19:** 698–700.
6. Livingston A, Waterman AE. Self induction of metabolism by ketamine in the rat. (Proceedings) *British Journal of Pharmacology* 1977; **60:** 296–7.
7. Kammerer RC, Schmitz DA, Hwa JJ, Cho AK. Induction of phencyclidine metabolism by phencyclidine, ketamine, ethanol, phenobarbital and isosafrole. *Biochemical Pharmacology* 1984; **33:** 599–604.
8. Pessayre D, Allemand H, Benoist C, Afifi F, François M, Henkman JP. Effect of surgery under general anaesthesia on antipyrine clearance. *British Journal of Clinical Pharmacology* 1978; **6:** 505–13.
9. Duvaldestin P, Mazze RI, Nivoche Y, Desmonts JM. Occupational exposure to halothane results in enzyme induction in anesthetists. *Anesthesiology* 1981; **54:** 57–60.

Anaesthesia, 1986, Volume 41, pages 582–585

The effects of continuous intravenous naloxone on epidural morphine analgesia

G. S. THIND, J. C. D. WELLS AND R. G. WILKES

Summary

Forty-five patients undergoing Caesarean section under epidural anaesthesia with bupivacaine were randomly allocated to three groups. Group 1 received 4 mg of epidural morphine immediately postoperatively and 2 mg naloxone by intravenous infusion for 12 hours postoperatively; group 2 was treated as group 1 but without naloxone infusion; group 3 received 10 mg morphine intramuscularly and 20 ml epidural saline after delivery of the baby. Epidural morphine 4 mg produced better postoperative analgesia than 10 mg of morphine intramuscularly ($p < 0{\cdot}001$) and the intravenous infusion of naloxone did not ablate the analgesic effects of epidural morphine. The incidence of itching and vomiting was higher in the epidural opioid groups ($p < 0.05$) and intravenous naloxone, although it reduced the severity of the itching, did not reduce its overall incidence. Respiratory depression was not detected in any of the three groups.

Key words

Anaesthetic techniques, regional; epidural.
Analgesics, narcotic; morphine.
Pain; postoperative.

Much has been written about the treatment of postoperative pain with epidural opioids since the original favourable report in 1979[1] and, with some exceptions,[2,3] the benefits have been widely recognised.[4] However, the occasional report of late respiratory depression and demonstration of rostral spread of the opioid within the cerebrospinal fluid (CSF)[5,6] have limited its use in general wards, where the benefits are most required.

Reports[7,8] that intravenous naloxone is an effective treatment of epidural opioid-induced respiratory depression have raised the possibility that its continuous administration might protect against this risk. However, it is first necessary to establish that such administration does not ablate the analgesic benefits. This study was designed to investigate the effects of continuous intravenous naloxone on epidural morphine analgesia. Patients undergoing elective Caesarean section under epidural anaesthesia with bupivacaine were chosen for this study, since they represent a homogeneous group and their postoperative care was undertaken by experienced nursing staff in a single ward with a resident anaesthetist immediately available. A further group was included, to compare epidural opioid analgesia to the standard practice at this hospital of intramuscular analgesia.

G.S. Thind, MB, ChB, FFARCS, Senior Registrar in Anaesthesia, J.C.D. Wells, MB, ChB, FFARCS, Consultant Anaesthetist, R.G. Wilkes, MB, ChB, FFARCS, Consultant Anaesthetist, Liverpool Maternity Hospital, Oxford Street, Liverpool, L7 7BN.

0003–2409/86/060582 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

Methods

This study was approved by the ethical committee of the Liverpool Women's and Maternity Hospitals. Forty-five patients consented to participate; their ages ranged from 18–36, their weights from 57–95 kg and their heights from 145–170 cm. All were unpremedicated and epidural anaesthesia was introduced at either the $L_{2/3}$ or $L_{1/2}$ interspace, using 18–26 ml of 0.5% bupivacaine with 1/400000 adrenaline. The patients were randomly divided into three groups of 15.

Group 1 received 4 mg of epidural morphine (morphine sulphate 2 mg in 10 ml saline) and one ml of intramuscular saline, immediately after delivery of the baby. One hour later, 0.4 mg (1 ml) naloxone was given intravenously and 1.6 mg (4 ml) added to 1 litre of Hartmann's solution, which was set to run intravenously over 12 hours.

Group 2 received drugs as in group 1, except that in lieu of naloxone, 1 ml and 4 ml of saline were given intravenously and into the Hartmann's solution respectively.

Group 3 received 20 ml of epidural saline and 10 mg (1 ml) of morphine intramuscularly, immediately after delivery of the baby. One hour after the epidural saline, 1 ml and 4 ml of saline were given intravenously and into the Hartmann's solution.

A consultant anaesthetist, who was not involved in the trial, drew a coded card from a shuffled pack to determine the allocation of a patient to a particular group. He drew up the appropriate drugs in four syringes, which were labelled only with the route by which their contents were to be administered. Thus, both nursing staff and investigator were blind as to which group a patient belonged to.

Patients were assessed formally by one of the investigators at 1, 2, 4, 6, 10–12, 18–20, and 24 hours post delivery. At these times, pain was assessed by use of a vertical 100-mm linear analogue scale, pruritus assessed using a similar scale, respiratory rate recorded and episodes of vomiting noted. Concomitantly, nursing staff made their own assessments hourly for the first 8 hours, then 2-hourly for the remaining 24 hours post delivery; they recorded the same items, but used defined terms of absent, mild, moderate or severe pain and itching.

All patients were prescribed cyclimorph 10 (morphine tartrate 10 mg, cyclizine tartrate 50 mg in 1 ml) 1 ml intramuscularly and paracetamol tablets 600 mg, which were given at the discretion of the nursing staff. Patients were asked to record their pain score immediately prior to administration of additional analgesia. Prochlorperazine 12.5 mg (1 ml) was prescribed, to be given by the nursing staff if the patient vomited more than once. Severe itching was treated by administration of 0.4 mg naloxone intravenously, followed by chlorpheniramine intramuscularly if this failed to effect satisfactory relief.

Most of the patients underwent Caesarean section either late morning or early afternoon, so that the first 10–12 hours post delivery were before midnight.

Results

All patients experienced satisfactory anaesthesia during their Caesarean sections and none required any additional opioid or sedative other than that prescribed by the trial. The three groups were well matched in respect of age, weight and height, and there was no statistical difference between them.

Pain

In the epidural morphine groups, only one patient (Table 1) received cyclimorph, which was given at 22 hours post delivery with a pain score of 36; no other patient recorded pain scores higher than 40 (Table 2). Paracetamol was given to five patients in group 1 and three in group 2 between 12 and 20 hours post delivery. In contrast, 14

Table 1. Number of intramuscular analgesic supplements given during first 24 hours after delivery. (Statistical analysis chi-square test).

	None	One	Two	Three	
Group 1	14	1	0	0	}$p < 0.001$
Group 2	15	0	0	0	
Group 3	1*	2	7	5	

*One patient in Group 3 refused opioid intramuscular injection despite a pain score of 62.

Table 2. Maximum pain scores during 24 hours after delivery or before analgesia.

	0–20	21–40	41–60	61–80	81–100
Group 1	12	3*	0	0	0
Group 2	11	4	0	0	0
Group 3	0	3	6	5	1

(94%) of the patients who received intramuscular morphine at delivery were given intramuscular cyclimorph within 6 hours postpartum; of these, 12 required repeated doses. Twelve recorded pain scores higher than 40, with six higher than 60 (Table 2). There was a significant difference between the pain scores of the group 3 patients compared with groups 1 and 2 ($p < 0.01$, analysis of variance).

Itching

Only one (7%) patient in group 3 (Table 3) experienced troublesome itching. In contrast, all except one patient who had received epidural morphine experienced some pruritus. Although the majority were not troubled by this symptom, three in group 2 required specific treatment. In one intravenous naloxone 0.4 mg produced satisfactory relief but in the other two additional chlorpheniramine 10 mg intramuscularly was necessary. Most of the cases in the epidural morphine groups occurred between the 4th to 10th hour after delivery and predominantly affected the face and trunk.

Table 3. Itching score during 24 hours after delivery or prior to therapy.

	Absent	Mild (<30)	Moderate (30–60)	Severe (>60)
Group 1	1	9	5	0
Group 2	0	9	3	3*
Group 3	7	7	1	0

* Note that three patients in Group 2 required treatment.

Vomiting

Vomiting occurred in 47% of patients in both groups 1 and 2 postoperatively, whereas only 7% of patients in group 3 did so (Table 4).

Table 4. Vomiting during 24 hours after delivery

	None	One	Two	Four	
Group 1	8	4	2	1	}$p > 0.1$
Group 2	8	3	3	1	
Group 3	14		1		}$p < 0.05$

Respiratory rate

The lowest recorded respiratory rate was similar in all three groups and none was less than 14 breaths/minute (Table 5).

Table 5. Lowest respiratory rate during 24 hours after delivery

	12	14	16	18	20
Group 1	0			9	6
Group 2	0	1	7	6	1
Group 3	0	1	2	6	6

Discussion

Our results indicate that in patients undergoing epidural Caesarean section under bupivacaine anaesthesia, 4 mg of morphine sulphate given via the epidural route provided much better postoperative pain relief than 10 mg intramuscularly. This is in accord with the reports of others[9] and is difficult to reconcile with those claiming only marginal differences.[2,3]

This study was designed to be double blind, but the nursing staff claimed that they were often able confidently to identify the route via which the opioid had been given by the quality of analgesia which existed when the local anaesthetic wore off. Their prejudice in favour of the epidural route may have accounted for some patients in group 3 receiving injections of cyclimorph 10 when patients in group 1 and 2 with similar pain scores did not. Interestingly, the one patient in group 3 who did not receive opioid supplementation suffered a maximum pain score of 62. She admitted to severe pain, but expressed strong determination to avoid intramuscular narcotics. This further underlines the fallibility of equating analgesic supplementation with degree of pain relief.[10]

The incidence of pruritus and vomiting was much higher in the epidural morphine groups. The cyclizine component of cyclimorph may have reduced the incidence of these side effects in group 3. Continuous intravenous naloxone in the dosage given in this study, while not reducing the overall incidence of pruritus and vomiting, effected a reduction in the severity of itching, although this was not statistically significant.

Respiratory depression, assessed by recording the respiratory rate, is an accepted method of detecting opioid induced respiratory depression,[11] and did not occur in this study, as was to be expected in a group of young, fit patients receiving relatively low doses of epidural morphine. Recently, however, serious doubts have been expressed,[12] about the use of respiratory rate alone as a means of detecting respiratory depression induced by opioids; periodicity of breathing appears to be a more sensitive measure.[13]

A continuous infusion of naloxone has been shown to reverse the effects of epidural morphine on bladder muscle tone,[14] but the dosages used to achieve this reversal were considerably higher than those used in this study. However, detrusor relaxation and analgesia appear to depend on direct spinal action of epidural opioids, which appears more resistant to naloxone reversal than respiratory depression, which occurs later. This is thought to represent rostral spread in the CSF[6] and is more likely to be reversed by naloxone.[15]

It is not possible from this study to be certain that the dose of naloxone used offers any protection against respiratory depression induced by 4 mg epidural morphine, although similar dosages were very effective in treating a reported case of respiratory depression after this dose of morphine given intrathecally.

Acknowledgments

Our thanks are due to all those colleagues who assisted, particularly Dr C. Charway and Dr P. Buckley. We are especially grateful to the nursing staff on our postoperative ward, without whose co-operation this work would have been impossible.

References

1. Behar M, Magora F, Olshwang D, Davidson JT. Epidural morphine in treatment of pain. *Lancet* 1979; **1:** 527–9.
2. Chambers WA, Mowbray A, Wilson J. Extradural morphine for the relief of pain following Caesarean section. *British Journal of Anaesthesia* 1981; **55:** 1201–3.
3. Crawford JS. Experiences with epidural morphine in obstetrics. *Anaesthesia* 1981; **36:** 207–9.
4. Stenseth R, Sellevold O, Brevik H. Epidural morphine for post-operative pain. Experience with 1085 patients. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 148–56.
5. Nielsen CH, Camporesi EM, Bromage PR, Bukowski EM, Durran DAC. CO_2 sensitivity after epidural and I.V. morphine. *Anesthesiology* 1981; **55:** A372.
6. Bromage PR, Camporesi EM, Durant PAC, Nielson CH. Rostral spread of epidural morphine. *Anesthesiology* 1982; **56:** 431–6.
7. Christensen V. Respiratory depression after extradural morphine. *British Journal of Anaesthesia* 1980; **52:** 841.
8. Reiz S, Westberg M. Side effects of epidural morphine. *Lancet* 1980; **2:** 203–4.
9. Rosen MA, Hughes SC, Shnider SM, Abboud TK, Norton M, Dailey PA, Curtis JD. Epidural morphine for the relief of postoperative pain after Caesarean delivery. *Anesthesia and Analgesia* 1983; **62:** 666–72.
10. Rutter DV, Skewes DG, Morgan M. Extradural opioids for postoperative analgesia. A double-blind comparison of pethidine, fentanyl and morphine. *British Journal of Anaesthesia* 1981; **53:** 915–20.
11. Malins AF, Goodman NW, Cooper GM, Prys-Roberts C, Bairds RN. Ventilatory effects of pre- and postoperative diamorphine. A comparison of extradural with intramuscular administration. *Anaesthesia* 1984; **39:** 118–25.
12. Camporesi EM, Nielsen CH, Bromage PR, Durant PAC. Ventilatory CO_2 sensitivity after intravenous and epidural morphine in volunteers. *Anesthesia and Analgesia* 1983; **62:** 633–40.
13. Arunasalam K, Davenport HT, Painter S, Jones JG. Ventilatory response to morphine in young and old subjects. *Anesthesia* 1983; **38:** 529–33.
14. Rawl N, Mölleforsk, Axelsson K, Lingardh G, Widman B. An experimental study of urodynamic effects of epidural morphine and of naloxone reversal. *Anesthesia and Analgesia* 1983; **62:** 641–7.
15. Jones RDM, Jones JG. Intrathecal morphine: naloxone reverses respiratory depression but not analgesia. *British Medical Journal* 1980; **281:** 645–6.

Anaesthesia, 1986, Volume 41, pages 586–588

The influence of nitrous oxide on oxyhaemoglobin dissociation and measurement of oxygen tension

M. V. SHAH, L. K. ANDERSON AND N. A. BERGMAN

Summary

There are conflicting reports of the effect of nitrous oxide on the oxyhaemoglobin dissociation curve. We have therefore determined P_{50} of haemoglobin in the presence of either nitrous oxide or nitrogen and studied the upper portion of the curve in greater detail. No significant differences in the oxyhaemoglobin dissociation curve were observed when nitrous oxide was substituted for nitrogen. The oxygen tensions measured in gas mixtures were not significantly different when determined simultaneously with a polarographic oxygen electrode and the mass spectrometer when nitrous oxide was used instead of nitrogen.

Key words

Blood; oxyhaemoglobin dissociation, mass spectrometry.
Gases; nitrogen, nitrous oxide.
Measurement techniques; polargraphy.

If the oxyhaemoglobin dissociation curve were shifted it would influence unloading of oxygen at the tissue level and might be sometimes clinically significant. Studies of the effects of nitrous oxide on oxyhaemoglobin dissociation have given inconsistent results. Smith and co-workers[1] studied this effect and showed a small rightward shift, which would improve oxygenation at the tissue level, whereas Fournier *et al.*[2] recently reported a shift to the left in the oxyhaemoglobin dissociation curve of 9 mmHg, which could compromise unloading of oxygen at the tissue level. In the light of this recent report, we re-examined the effects of nitrous oxide on oxyhaemoglobin dissociation. Since Fournier *et al.* also reported systematically higher oxygen tension ($P\text{O}_2$) readings with their $P\text{O}_2$ electrode in the presence of nitrous oxide, we also examined the effect of nitrous oxide on a polarographic oxygen electrode.

Methods

Venous blood samples were obtained from five volunteers. Pairs of oxyhaemoglobin dissociation curves were plotted from each sample, using a Hem-O-Scan analyser (American Instrument Co., Silver Spring). This instrument continuously measures the oxygen tension and saturation of haemoglobin with oxygen, at 37°C, as a thin film of blood (2×10^{-6} litre) equilibrates with a known gas mixture. A continuous oxyhaemoglobin dissociation curve is automatically plotted.

A normal dissociation curve was plotted for each sample (the control curve) as follows. The blood was first deoxygenated by flushing the

---

M.V. Shah, MB, BS, FFARCS, Visiting Assistant Professor, L. K. Anderson, MD, Resident, N.A. Bergman, MD, Professor, The Oregon Health Sciences University, Department of Anesthesiology, 3181 S.W. Sam Jackson Park Road, Portland, Oregon 97201, USA.

0003–2409/86/060586 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

chamber of the instrument with a gas mixture of nitrogen (95%) and carbon dioxide (5%) and the zero point was adjusted. A gas mixture of nitrogen (70%), carbon dioxide (5%) and oxygen (25%) was then introduced into the chamber, the sensitivity was adjusted and a normal dissociation curve was then obtained. A second dissociation curve was obtained as above, substituting nitrous oxide for nitrogen. The gas mixtures used were from certified cylinders (Airco Medical Products, Portland, Oregon) whose composition was confirmed with a mass spectrometer. The P_{50} was read from each of the curves. Five pairs of P_{50} were thus obtained.

The upper portion of the oxyhaemoglobin dissociation curve is usually more relevant during anaesthesia. This aspect was therefore studied by an alternative method. Mixtures of oxygen, carbon dioxide, and nitrogen or oxygen, carbon dioxide and nitrous oxide were generated with an anaesthetic machine. The exact composition of the mixture was adjusted and continuously monitored with a Perkin Elmer mass spectrometer (Pomona CA), which was calibrated with commercially obtained and analysed gas mixtures. Twenty-four fresh, heparinised, human blood samples (10 ml) were obtained from twelve patients (ASA 1), who were anaesthetised with nitrous oxide and oxygen. These samples were equilibrated for a minimum of 30 minutes in a Dynex tonometer (Analytical Products, Inc., Belmont, CA) at 37°C with the various mixtures. Then $P\mathrm{O}_2$ and carbon dioxide tension ($P\mathrm{CO}_2$) of the effluent tonometer gas and pH, $P\mathrm{O}_2$ and $P\mathrm{CO}_2$ of an aliquot of the equilibrated blood were measured using a Corning 168 Blood Gas Analyser maintained at 37°C. Haemoglobin saturation of equilibrated blood was measured using a reflectance oximeter (American Optical Co.) on the remaining blood in the aliquot. Predicted haemoglobin saturation was then obtained from the nomograms of Kelman and Nunn[3] at the equilibrating $P\mathrm{O}_2$, as measured with the mass spectrometer. Measured and predicted haemoglobin saturation for each sample were then corrected for pH and base excess, again using the nomograms of Kelman and Nunn. Twelve values of $P\mathrm{O}_2$ using nitrogen (the control group) and twelve values of $P\mathrm{O}_2$ using nitrous oxide (the study group) were obtained. The differences in $P\mathrm{O}_2$ between the measured and standard curves were calculated.

The influence of nitrous oxide on the oxygen electrode was determined as follows. Mixtures of oxygen with nitrogen or nitrous oxide were generated from an anaesthetic machine and simultaneously delivered to a blood gas analyser (Corning 168) and a mass spectrometer, both previously calibrated. The simultaneous measurements of $P\mathrm{O}_2$ were recorded from the polarographic oxygen electrode and the mass spectrometer.

The differences between the pairs of measurements obtained from the first and third parts of the study were analysed using Student's *t*-test for paired data. The differences in $P\mathrm{O}_2$ between the measured and the standard curve from the control group and the study group were analysed using Student's *t*-test for unpaired data.

Results

The mean P_{50} measured from the oxyhaemoglobin dissociation curves obtained with the gas mixture containing nitrous oxide was 3.68 kPa (SD 0.26). The mean for the control group with nitrogen was 3.80 kPa (SD 0.13). The differences between the groups were not significant (Table 1).

The results from the second part of the study are depicted in Fig. 1, which shows the standard oxyhaemoglobin dissociation curve in the clinical range of $P\mathrm{O}_2$ and the measured saturations in the presence of either nitrous oxide or nitrogen. The $P\mathrm{CO}_2$ in equilibrating gas ranged from 4.21 to 5.53 kPa. The $P\mathrm{O}_2$ ranged from 6.45–13.29 kPa. Measured haemoglobin saturation was from 85–96% (Fig. 1). When the differences in saturation were analysed from the standard curve, there was a small increase from the standard curve in the presence of nitrogen, 0.57% (SD 2.47) and an

Table 1. The P_{50} of five volunteers, kPa, from oxyhaemoglobin dissociation curves plotted in the presence of nitrogen and in the presence of nitrous oxide.

P_{50} measured in the presence of	1	2	3	4	5	Mean (SD)*
Nitrogen	3.68	3.68	3.95	3.75	3.95	3.80 (0.13)
Nitrous oxide	3.62	3.49	4.14	3.62	3.55	3.68 (0.26)

*$p > 0.1$.

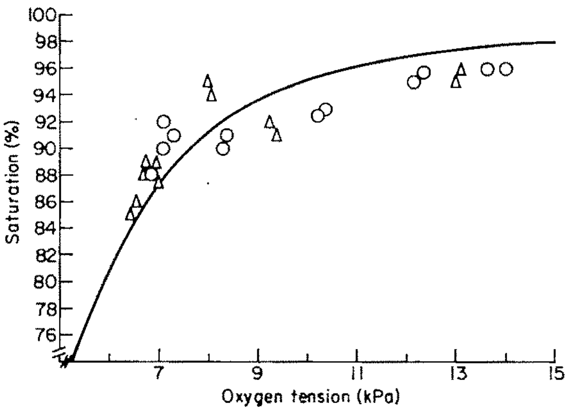


Fig. 1. The measured oxygen tension ($P\mathrm{O}_2$) values plotted in relation to the standard oxyhaemoglobin dissociation curve.[3] (○), nitrous oxide; (△), nitrogen.

even smaller increase in the presence of nitrous oxide, 0.15% (SD 2.75). These differences are small and actually show a slight shift to the right in the presence of nitrous oxide when compared to nitrogen. However, these groups were not found to be significantly different from each other.

When the $P\mathrm{O}_2$ measured by our polarographic oxygen electrode was compared to the $P\mathrm{O}_2$ measured by our mass spectrometer, the ratio was 0.986 in the presence of nitrogen, but was 1.012 in the presence of nitrous oxide. This difference of 0.026 was not significant ($p > 0.1$).

Discussion

A significant shift to the left of the oxyhaemoglobin dissociation curve caused by nitrous oxide could influence the choice of this gas in the practice of anaesthesia. Our data indicate that there is no significant change in the oxyhaemoglobin dissociation curve when nitrous oxide is substituted for nitrogen in equilibrating mixtures, both when the P_{50} is measured and when the upper end of the dissociation curve is examined. The results agree with those published by Prime.[4]

Our results disagree with those of Fournier and Major.[2] We encountered no difficulty with zeroing of the Hem-O-Scan oxygen dissociation analyser and obtained normal dissociation curves, even in the presence of nitrous oxide. A small effect of nitrous oxide on the polarographic oxygen electrode[5] may be expected to cause a small shift to the right of the measured oxyhaemoglobin dissociation curve, as observed by Smith *et al.*[1]; however, we failed to detect a significant effect in this respect. We are unable to explain the discrepancy between our results and those of Fournier and Major.

We conclude that nitrous oxide does not significantly shift the oxyhaemoglobin dissociation curve.

Acknowledgments

We are grateful to Professor R. Koler and Mrs M. Jones for the use of the Hem-O-Scan oxyhaemoglobin analyser and their help in its application to the study.

References

1. SMITH TC, COLTON ET, BEHAR MG. Does anesthesia alter hemoglobin dissociation? *Anesthesiology* 1970; **32:** 5–10.
2. FOURNIER L, MAJOR D. The effect of nitrous oxide on the oxyhaemoglobin dissociating course. *Canadian Anesthetists' Society Journal* 1984; **31:** 173–7.
3. KELMAN GR, NUNN JF. Nomograms for correction of blood $P\mathrm{O}_2$, $P\mathrm{CO}_2$, pH, and base excess for time and temperature. *Journal of Applied Physiology* 1966; **21:** 1484–90.
4. PRIME FJ. Oxygen dissociation curves of whole blood in the presence of anaesthetic gases. *British Journal of Anaesthesia* 1951; **23:** 171–9.
5. EVANS MC, CAMERON IR. Oxygen electrodes sensitive to nitrous oxide. *Lancet* 1978; **2:** 1371.

Anaesthesia, 1986, Volume 41, pages 589–595

Propofol and alfentanil infusion

A comparison with methohexitone and alfentanil for major surgery

B. KAY

Summary

In 42 patients undergoing major surgery, anaesthesia was induced by intravenous alfentanil 10 μg/kg together with methohexitone 1.5 mg/kg or propofol 2 mg/kg. An infusion of six times these doses per hour was then started; the rate was varied subsequently as indicated by the monitoring of arterial blood pressure, heart rate, EEG and frontalis electromyogram. The mean duration of infusion was 76.7 minutes for propofol and 74.5 minutes for methohexitone and the infusion was stopped about 10 minutes before the end of surgery in each group. The induction dose differed, but the total dose requirement for the two drugs was similar. In every case, anaesthesia was satisfactory. Methohexitone caused a significant rise in mean pulse rate throughout anaesthesia ($p < 0.05$, paired t-test). There was no change in mean pulse rate during propofol infusion. The dose of alfentanil used provided excellent control of autonomic reflexes, with negligible respiratory depression. Naloxone was not required. Propofol provided better anaesthesia than methohexitone, with fewer side effects ($p < 0.05$, Chi squared test), easier control of the level of narcosis and faster recovery ($p < 0.001$, t-test after log transformation).

Key words

Anaesthetics, intravenous; methohexitone, propofol.
Analgesics, narcotic; alfentanil.

Total intravenous anaesthesia was first popularised by Savege *et al.*[1] using Althesin. Although improved gas scavenging has removed one of the first indications for the technique, and Althesin is no longer available, the introduction of new hypnotic and analgesic drugs and improved monitoring has maintained an interest in providing anaesthesia by using agents with more selective effects than the volatile anaesthetics. Experience has shown that intravenous techniques may be at least as acceptable as those using anaesthetic vapours.[2]

Propofol is a new intravenous anaesthetic which appears to have advantages over currently available drugs for maintenance of anaesthesia by infusion. It has a smooth and rapid onset of effect, similar to that of thiopentone,[3] but has a very fast rate of metabolic clearance from the blood.[4] An earlier preparation of propofol in Cremophor E was shown to provide excellent anaesthesia for major surgery when given by infusion,[5] but this has now been replaced by an emulsified formulation of propofol.

Alfentanil has the fastest onset and shortest duration of effect of any opioid. It has an elimination half-life of 96 minutes[6] and was shown to be a suitable analgesic component of anaesthesia for major surgery when given by

---

B. Kay, DMSc, MB, ChB, FFARCS, Reader in Anaesthesia, University of Manchester, University Hospital of South Manchester, Withington, Manchester M20 8LR.

0003–2409/86/060589 + 07 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

infusion together with etomidate.[7] However, etomidate infusion anaesthesia may cause unwanted side effects and occasionally poor recovery, particularly due to myoclonia persisting after recovery of consciousness.[7,8]

Methohexitone, with a rapid onset of effect and a faster rate of elimination than thiopentone, is extensively used for outpatient anaesthesia and for maintenance of anaesthesia of short duration by intermittent injection. Mixtures of methohexitone with alfentanil and propofol with alfentanil have been used by this method for outpatient cystoscopy,[9] but the use of such mixtures given by infusion for major surgery has not been reported.

It was of interest, therefore, to examine the efficacy of an infusion of propofol and alfentanil for major surgery, using a simple one syringe technique similar to that employed for the study of etomidate and alfentanil infusion[7] and to compare the results obtained with those using methohexitone and alfentanil.

Method

Studies were carried out on 42 patients of ASA grades 1 or 2 undergoing major surgery. All the patients gave their written informed consent to the trial, which was approved by the hospital ethical committee. A continuous ECG (CM5) display was started in the anaesthetic room; the unipolar electroencephalogram (EEG), mean frequency and amplitude, frontalis electromyogram (EMG) amplitude, pulse rate and mean systolic and diastolic arterial blood pressure (Dinamap) were recorded by ABM (Datex), as were the capnograph and neuromuscular transmission (train-of-four) instituted after induction of anaesthesia.

No premedication was given. Anaesthesia was induced using alfentanil 10μg/kg, immediately followed by methohexitone 1%, approximately 1.5 mg/kg, or propofol 1%, about 2 mg/kg; these were randomly allocated and given over 20 seconds, followed by alcuronium 15 mg. All drugs were given into a single channel Y-can inserted into a forearm vein and were immediately followed by an infusion of the hypnotic used for induction, mixed with alfentanil in a 50-ml syringe, given by the same route. The syringe was filled with 300 mg propofol 1% together with alfentanil 1.5 mg, or 300 mg methohexitone 1% and alfentanil 2 mg. A Fresenius syringe pump modified to give up to 150 ml/hour was used to give six times the doses used for induction per hour initially. The trachea was intubated and the lungs ventilated with approximately 40% oxygen in air to maintain normocapnia.

Alcuronium 5 mg was given as indicated by increasing neuromuscular transmission. The infusion rate was increased and/or a bolus dose of the anaesthetic mixture given if an autonomic or somatic nervous reflex response to surgery was observed. The rate was usually reduced by approximately one third when mean EEG frequency fell to 7 or 8 Hz, usually 20–30 minutes after induction of anaesthesia. Infusion was stopped 10 minutes before the expected end of surgery. A bolus of 10 mg propofol or methohexitone was given if a rise in frontalis EMG indicated that the patient was about to recover consciousness before surgery was complete.

The time to onset of spontaneous ventilation following the start of tachycardia after atropine 1 mg and neostigmine 2.5 mg were given together intravenously during skin closure, was noted. The peak end tidal carbon dioxide concentration was then recorded, and the trachea extubated. The patient was subsequently asked at 15-second intervals to protrude the tongue and the time when this request was complied with was noted.

Any side effects or complications observed during induction, maintenance or recovery from anaesthesia were noted. During induction, the patient was asked 'Are you comfortable?' and if pain was reported, its severity assessed. After recovery, the patient was asked if he would like to receive the same anaesthetic again and the anaesthetist graded the ease of control of anaesthesia and quality of recovery as good, adequate or poor. A specific enquiry regarding awareness during surgery was made.

Results

The patient demographic data are given in Table 1. The majority of operations performed were upper abdominal (mainly gastric or cholecystectomy). Hysterectomy or other lower abdominal surgery was performed on seven patients who received methohexitone and six in the propofol group, and thyroid surgery on two patients who received propofol and one who received methohexitone. Table 2 records the

Table 1. Patient demography; means (SEM)

Groups	*n*	Age (years)	Weight (kg)	Sex
Propofol	21	44.7 (2.2)	69.5 (1.9)	16 F
Methohexitone	21	43.6 (3.1)	67 (2.5)	13 F

Table 2. Mean durations (SEM) of administration (I), surgery and anaesthesia (A) (induction to end of surgery), minutes.

Group	Infusion	Surgery	Anaesthesia	A − I
Propofol	76.7 (7.7)	71.9 (0.4)	85.8 (8.2)	9.1 (1)
Methohexitone	74.5 (8.6)	69.8 (8.9)	83.9 (8.7)	9.4 (1)

Table 3. Mean (SEM) drug dosage, mg.

Group	Induction	Total	Rate mg/kg/minute
Propofol	131.7 (3.8)*	762.2 (58)	0.143
Methohexitone	105 (4.9)*	703.8 (61)	0.141
Alfentanil			
(with propofol)	3.75 i.e. 0.7 μg/kg/minute		
(with methohexitone)	4.65 i.e. 0.93 μg/kg/minute		

*$p < 0.05$, *t*-test.

mean duration of administration of anaesthetic drugs, from induction until end of infusion or the ultimate bolus dose, the mean duration of surgery and the mean duration from the last dose of anaesthetic until the end of surgery in each group. There are no differences between the groups. The mean doses of alfentanil, propofol and methohexitone used and the rates of administration are given in Table 3. The dose of propofol used for induction of anaesthesia was significantly greater than that of methohexitone, ($p < 0.05$, *t*-test) but there were no differences between the groups in overall dosage or rate of use of the intravenous anaesthetics or alfentanil.

There were no major problems in using the technique for major surgery. Conditions for surgery were completely acceptable at all times and patients were generally very pleased with the technique. All patients who received propofol stated that they would choose to have the same anaesthetic again. Five of the patients who received methohexitone indicated that they would choose to have the same anaesthetic again. Five of the patients who received methohexitone indicated that they would not choose the same anaesthetic again, due to slow or confused recovery or side effects during induction of anaesthesia. All patients were unconscious throughout surgery. There were three instances of technical problems; in one case the cannula became dislodged from the vein and the methohexitone–alfentanil mixture extravasated; in a second case the anaesthetic infusion became detached from the main infusion; in the third instance, the pump (in this case a Vickers Treonic 3) failed to deliver the set rate. In each case the patient monitoring gave early warning of the infusion failure which was rapidly corrected (in the case of the pump failure, by manual infusion).

There was a significant difference in the incidence of side effects in the groups ($p < 0.05$, Chi squared test). In the methohexitone group, nine patients suffered a total of 11 side effects during induction of anaesthesia; four had pain during injection, three myoclonia and four hiccup; another patient was confused during recovery. In the propofol group two patients felt pain during injection. There were no side effects during maintenance of anaesthesia in either group.

The cardiovascular effects of anaesthesia are illustrated in Figs 1 and 2. In both groups there was a similar, significant fall in systolic and diastolic arterial pressure 2 and 3 minutes after induction of anaesthesia ($p < 0.05$, paired *t*-test), which was reversed by tracheal intubation, although the mean values did not exceed control levels. Subsequently, mean systolic values in both groups and diastolic values in the propofol group fell below control levels at some times. There were significant differences between the groups 4 minutes after intubation, and 15 minutes after

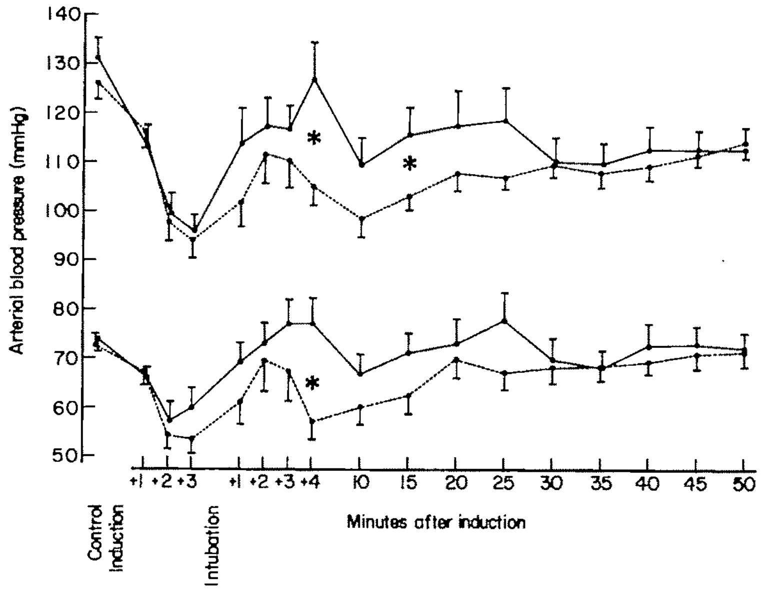


Fig. 1. Mean systolic and diastolic arterial blood pressure during the first 50 minutes of anaesthesia (SEM). ——, Methohexitone; ------, propofol. *Difference between groups $p<0.05$, t-test.

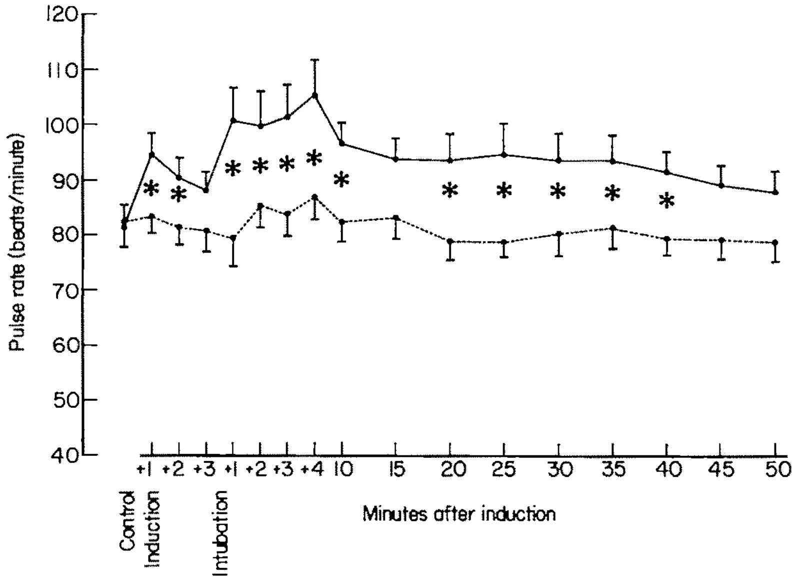


Fig. 2. Mean pulse rate during the first 50 minutes of anaesthesia (SEM). ——, Methohexitone; ------, propofol. *Difference between groups $p<0.05$, t-test. No means during propofol anaesthesia differ from control, all means during methohexitone anaesthesia are greater than control, $p<0.05$, paired t-test.

induction of anaesthesia; in each case, the values were lower in the propofol group ($p<0.05$, t-test).

During propofol/alfentanil anaesthesia, at no time did mean cardiac rate differ significantly from pre-induction levels, but during methohexitone/alfentanil anaesthesia every mean value was significantly greater than control levels ($p<0.05$, paired t-test). There was a significant difference between the groups at most times ($p < 0.05$, *t*-test). The increases in heart rate and arterial blood pressure following tracheal intubation were greater and persisted longer after methohexitone than after propofol.

Control of level of narcosis and autonomic nervous response to surgical stimulation was more readily maintained by propofol and alfentanil than by methohexitone and alfentanil. Increases in systolic arterial blood pressure in excess of 10% greater than pre-anaesthetic values were rare, as were instances of a heart rate over 100 beats/minute in the propofol group, in which ease of control was classified as good in 19 patients and adequate in two. In the methohexitone group, control was considered to be good in 13 patients, adequate in five and difficult in three. An increase in infusion rate, or bolus injections in addition to the infusion were required in seven of the patients who received methohexitone and in four of those who received propofol; the extra dosage involved resulted in a similar overall dose requirement in each group.

After infusion was stopped, a mean time of about 9 minutes before the end of surgery in each group, three patients required bolus doses of methohexitone because of incipient awareness during surgery, compared with seven patients requiring propofol; this suggests a faster recovery after the latter drug. This was confirmed by the average time to protrusion of the tongue on request, measured from the time of administration of the final dose of the drug; this was 12.4 (range 4–24) minutes after propofol and a significantly longer 20.9 (4–57) minutes after methohexitone ($p < 0.001$, *t*-test after log transformation).

Recovery was assessed by the anaesthetist as good in 20 patients, adequate in one after propofol, but good in only six patients, adequate in nine and poor (because of prolonged unconsciousness) in six after methohexitone ($p < 0.001$, Chi squared test).

There was, however, no difference between the groups in the time to onset of spontaneous breathing after reversal of neuromuscular block; this was, on average, 59 seconds (range 0–3.5 minutes) after propofol and and 61 seconds (0–6 minutes) after methohexitone. The mean maximum end tidal $P\mathrm{CO}_2$ levels observed in each group during established breathing, before extubation, were similar and the maximum values recorded were also similar, indicating a degree of respiratory depression that was acceptable. After propofol and alfentanil, the average and range were 5.6 (4.8–6.5 kPa) and after methohexitone and alfentanil 5.4 (3.6–6.9 kPa).

Discussion

This investigation clearly confirmed that the theoretical advantages of propofol over methohexitone as an intravenous anaesthetic are apparent in clinical practice. The smooth induction characteristics of propofol were observed and provided an onset of unconsciousness that was generally preferred to induction by methohexitone. Both drugs maintained unconsciousness without side effects in these paralysed, ventilated patients, but control was easier with propofol, with fewer interventions in the form of bolus increments than were required with methohexitone. In three patients who received methohexitone, rises in pulse rate and frontalis EMG required numerous supplementary doses of methohexitone and alfentanil to be given in rapid succession before the signs of adrenergic nervous activity and incipient awareness seen at onset of surgery were abolished. Recovery was faster after propofol than after methohexitone, perhaps predictably in view of the rate of elimination of the drugs from the body; this confirms experiences with propofol and alfentanil and methohexitone and alfentanil in shorter anaesthetics.[9]

The dosage of each drug required was easily ascertained by the monitoring employed. Overdosage, which produced an unwanted intensity of narcosis, was seen as a decreasing mean amplitude and frequency of the EEG. Underdosing produced the reverse effect, culminating in a sharply rising frontalis EMG with impending consciousness. Thus, dosage of hypnotic drug could be minimised. Stopping the infusion before the end of surgery, using a bolus if required to prevent awareness during surgery, generally allowed very rapid recovery after the completion of surgery, in the case of propofol comparable with recovery after nitrous oxide and fentanyl.

The effectiveness of alfentanil in controlling autonomic (and to some extent somatic) reflex nervous responses to surgery was excellent, as can be seen from Figs 1 and 2. The amounts infused, although in line with the author's previous practice,[7,9] were smaller than those frequently recommended[10,11] and did not cause clinically significant respiratory depression after reversal of neuromuscular blockade.

The chemical and pharmacokinetic interactions that may occur when alfentanil is administered together with propofol or methohexitone were not considered and were not apparent clinically. The agents had been used together in an earlier study, but with little physical admixture.[9] The very low water solubility of propofol would make rapid chemical changes unlikely, but destabilisation of the emulsion such as occurs with mixtures of propofol and atracurium (Higgins, B, personal communication) is possible. Such a change was not visually apparent in the present study, where the maximum duration of admixture of propofol and alfentanil was approximately 30 minutes.

A pharmacokinetic interaction between propofol and fentanyl, resulting in plasma concentrations of propofol that are greater than predicted has been reported.[5,10] However, the higher than expected plasma concentrations did not appear to increase the clinical effect of propofol. This apparent interaction might be due to changes in the elimination or distribution of propofol by fentanyl, and it would be of interest to ascertain whether similar interactions occur between propofol and alfentanil. However, despite the similarities of pharmacological effects of alfentanil and fentanyl, the pKa, pH and distribution in the body are so dissimilar as to make any inferences concerning similar interactions occur between propofol and alfentanil.

The possibility of alfentanil being less available because of absorption into the emulsion exists, and would require a bio-assay to detect it. The present study offered evidence that such an effect is clinically insignificant, as the rate of use of alfentanil was similar to earlier experiences.

The pharmacokinetics of propofol indicate that after intravenous injection, there is a rapid distribution of the drug from blood into tissue, followed by fast metabolic clearance ($t_{1/2}$ approximately 45 minutes) from the blood; a final phase of slow elimination of propofol ($t_{1/2}$ about 280 minutes) probably correlates with a slow return of the drug from poorly perfused fat into the blood.[4] Thus, accumulation of propofol is to be expected during continuous infusion at a fixed rate, resulting in higher than predicted blood concentrations[12] and slower recovery[13] than after a bolus injection of the drug. It is therefore important to use the best monitoring of intensity of narcosis and potential awareness available, to minimise the total dose of propofol infused (and therefore the quantity of drug accumulated in poorly perfused fat) and to allow the infusion to be stopped well before the end of surgery. The drug can then be given according to patient responses and plasma concentrations allowed to fall towards the end of surgery, so that waking occurs soon after surgery is complete. A bolus of propofol can be utilised to raise plasma concentration rapidly and to maintain unconsciousness should waking appear to be imminent during surgery; the subsequent fall in plasma concentration due to redistribution should then be rapid, with waking occurring only after a few minutes. Such a method of application is also appropriate for alfentanil, rather than the use of a predetermined infusion regimen to maintain a theoretical therapeutic plasma concentration through to the end of surgery.[14] The problem of clinically important respiratory depression was thereby avoided in the present study, which also demonstrated that the one syringe technique used allows the theoretical suitability of alfentanil and propofol for infusion anaesthesia to be simply and conveniently translated into effective clinical use.

References

1. Savege TM, Ramsay MAE, Curran JPJ, Cotter J, Walling PT, Simpson BR. Intravenous anaesthesia by infusion. A technique using alphaxolone/alphadolone (Althesin) *Anaesthesia* 1975; **30:** 757–64.
2. Waldron HA, Cookson RF. Use of a viewdata system to collect data from a multicentre clinical trial in anaesthesia. *British Medical Journal* 1984; **289:** 1059–61.
3. Nightingale P, Petts HV, Healy TEJ, Kay B, McGuinness K. Induction of anaesthesia with propofol ('Diprivan') or thiopentone and interactions with suxamethonium, atracurium and vecuronium. *Postgraduate Medical Journal* 1985; **61**, Supp 3: 31–4.
4. Cockshott ID. Propofol ('Diprivan') pharmacokinetics and metabolism—an overview. *Postgraduate Medical Journal* 1985; **61**, Suppl 3: 45–50.
5. Kay B, Verniquet AJW. Disoprofol and fentanyl for total intravenous anaesthesia. Abstracts Vol. I and II, *8th World Congress 1984 Anaesthesiologists*. Egay LM, DeLa Cruz-Odi M, Eds. World Federation of the Society of Anaesthesiologists, Manila, Philippines.
6. Bower S, Hull CJ. Comparative pharmacokinetics of fentanyl and alfentanil. *British Journal of Anaesthesia* 1982; **54:** 871–7.

7. Kay B. Etomidate and alfentanil infusion for major surgery. *Acta Anaesthesiologica Belgica* 1984; **35:** 19–24.
8. Kay B, Rolly G. Total intravenous anaesthesia with etomidate. 3. Experience with adults. *Acta Anaesthesiologica Belgica* 1977; **28:** 157–60.
9. Kay B, Healy TEJ. Propofol ('Diprivan') for outpatient cystoscopy. Efficacy and recovery compared with Althesin and methohexitone. *Postgraduate Medical Journal* 1985; **61,** Supp 3: 108–14.
10. Schuttler J, Stoeckel H, Wilms M, Schwilden H, Lauven PM. Ein Pharmakokinetisch begrundetes Infusionmodelle für Etomidat zur Aufrechterhaltung von Steady State Plasmaspiegeln. *Anaesthetist* 1980; **29:** 662–6.
11. Steegers PA, Booij LHDJ, Pelgrom R. Continuous infusion of alfentanil. *Acta Anaesthesiologica Belgica* 1982; **33:** 81–7.
12. Schuttler J, Stoeckel H, Schwilden H. Pharmacokinetic and pharmacodynamic modelling of propofol ('Diprivan') in volunteers and surgical patients. *Postgraduate Medical Journal* 1985; **61,** Supp 3: 53–4.
13. Gepts E, Claeys AM, Camu F. Pharmacokinetics of propofol ('Diprivan') administered by continuous intravenous infusion in man. A preliminary report. *Postgraduate Medical Journal* 1985; **61,** Suppl 3: 51–2.
14. Kay B. (Correspondence) *Acta Anaesthesiologica Belgica* 1984; **35:** 246–8.

Anaesthesia, 1986, Volume 41, pages 596–599

CASE REPORT

Peri-operative management of carcinoid syndrome using ketanserin

K. HOUGHTON AND J. A. CARTER

Summary

This report describes the successful use of ketanserin, a 5-HT_2 receptor antagonist, for the acute control of systemic blood pressure in a patient with the carcinoid syndrome, undergoing hepatic artery embolisation. Serial measurements of plasma 5-hydroxyindoles, platelet 5-hydroxytryptamine and plasma catecholamines are also given.

Key words

Blood pressure; carcinoid.
Hormones; catecholamines, ketanserin.

Ketanserin is a drug which binds to 5-hydroxytryptamine (5-HT_2) type 2 receptors and is known to have an acute hypotensive effect.[1,2] It has been stated that in therapeutic doses, the effects of amines other than 5-HT are not blocked and central side effects are absent.[1] However, it is also bound to a lesser extent to histamine (H_1), alpha-1-adrenergic receptors[3] and possibly to D-receptors in smooth muscle[4] and side effects are seen in the higher therapeutic doses.[5] Its use results in a decrease in pulmonary artery pressure, pulmonary wedge pressure, right atrial pressure and total peripheral resistance.[1]

Ketanserin may reduce systemic blood pressure by 5-HT_2 receptor blockade, by preventing amplification of alpha-1-adrenergic stimulation by 5-HT,[6] or by alpha-1-adrenergic antagonism.[7-9]

Ketanserin has been used orally to treat symptoms of carcinoid syndrome and intravenously in the management of a patient with carcinoid syndrome undergoing laser-photoresection of a bronchial metastasis.[10] Hepatic arterial embolisation is used to control symptoms of the malignant carcinoid syndrome.[11] We report the use of ketanserin for acute control of blood pressure during and after this procedure, with serial measurements of plasma 5-hydroxyindoles (5-HI), platelet 5-HT and plasma catecholamine levels.

Case history

A 55-kg-female aged 67 years had undergone a right hemicolectomy for histologically proven ileocaecal carcinoid tumour 5 years previously. She now presented with frequent attacks of diarrhoea and facial flushing, hepatomegaly and a urinary 5-hydroxyindole acetic acid (5HIAA) level of 400 μmol/litre (normal < 35 μmol/litre). Systemic arterial blood pressure was 130/80 mmHg. Ultrasound liver scan demonstrated multiple metastases, and so hepatic artery embolisation was proposed. Pre-operatively, she

---

K. Houghton, MB, ChB, FFARCS, Registrar, J.A. Carter, MB, BS, FFARCS, Senior Registrar, Department of Anaesthesia, Southmead Hospital, Bristol.

0003–2409/86/060596 + 04 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

received cyproheptadine (a histamine and non-selective 5-HT receptor blocker) 4 mg tds orally for 48 hours. Intravenous methylprednisolone 1 g, flucloxacillin 500 mg, metronidazole 1 g, tobramycin 120 mg and an infusion of aprotonin 50 000 units/hour were given immediately pre-operatively as currently recommended.[11] Intra-arterial and central venous cannulae were inserted for continuous monitoring and sampling.

The hepatic artery arteriogram caused a slight transient rise in blood pressure, but embolisation of the hepatic artery with Gelfoam caused an immediate rapid rise in systemic blood pressure from 160/80 to 204/104 mmHg, tachycardia, facial flushing and nausea. (Fig. 1). Ketanserin 10 mg intravenously effected a rapid immediate decrease in blood pressure to 150/90 mmHg with resolution of flushing and a fall in heart rate. Ten minutes later a further hypertensive episode was treated with ketanserin 5 mg and blood pressure fell rapidly from 210/104 mmHg to 120/80 mmHg. Subsequently, arterial and central venous pressures fell further and one unit of human plasma protein fraction was infused.

After embolisation, aprotonin, antibiotic therapy and cyproheptadine were continued. Five hours after embolisation, blood pressure rose again and ketanserin 5 mg effected a fall from 190/95 to 140/67 mmHg within 60 seconds. A continuous infusion of ketanserin at 10 mg/hour maintained pressure at this level. When this was discontinued, blood pressure immediately rose to 160/70 mmHg. The following day, two further hypertensive episodes occurred which responded to phentolamine 5 mg intravenously. Thereafter, systemic blood pressure settled at 110/70 mmHg.

Baseline samples were taken for plasma 5-HI, platelet 5-HT and plasma catecholamine levels and at 1, 3, 5 and 10-minute intervals following hepatic artery embolisation. The assay used for plasma 5-HI and platelet 5-HT levels was a

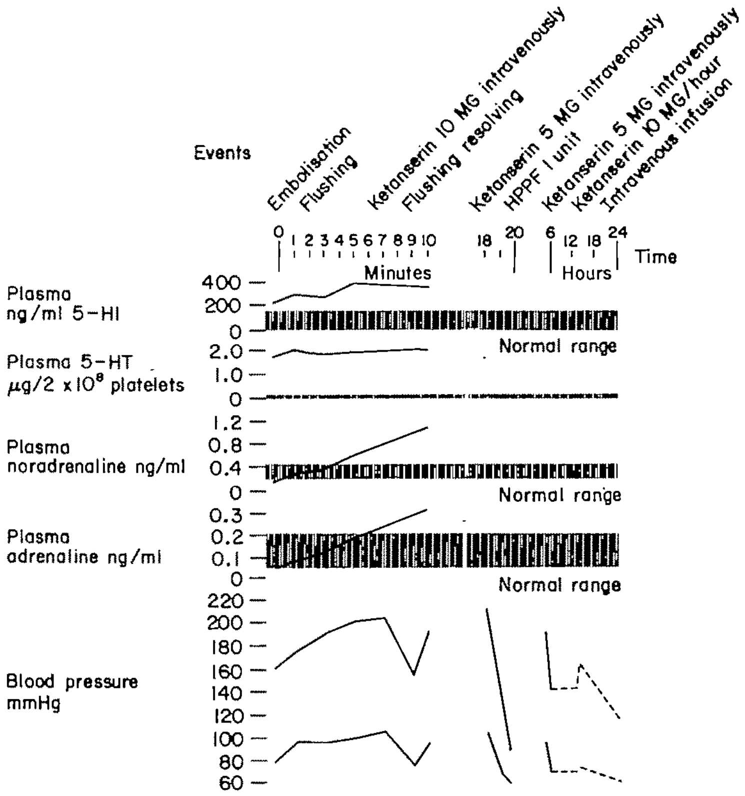


Fig. 1. Plasma 5-hydroxyindoles (5-HI), plasma 5-hydroxytryptamine (5-HT) plasma noradrenaline, adrenaline and diastolic and systolic blood pressure during the course of hepatic artery embolisation.

Table 1

Time (minutes)	Event	Plasma 5-HI (ng/ml)	Platelet 5-HT (μg/2 × 10^8 platelets)	Plasma noradrenaline (ng/ml)	Plasma adrenaline (ng/ml)	Arterial blood pressure (mmHg)	Pulse rate (beats/minute)
	Pre-embolisation	230	1.84	0.15	0.05	160/80	75
0	Embolisation					170/80	95
1	1-minute sample	299	2.02	0.30	0.09	175/95	105
3	3-minute sample	284	1.87	0.37	0.13	190/95	115
5	5-minute sample	383	1.97	0.60	0.19	200/100	100
7	Ketanserin 10 mg iv					204/104	102
9						155/75	95
10	10-minute sample	349	2.06	1.07	0.31	190/95	105
18	Ketanserin 5 mg iv					210/104	104
20						130/65	85
29	1 unit HPPF					85/55	70
5 hour	Ketanserin 5 mg iv					190/95	
	Ketanserin 10 mg/hour					140/67	
	Ketanserin discont.					160/70	
24 hour	24-hour sample	276	1.36			110/60	

Normal values: plasma adrenaline:0.05–0.2 ng/ml; plasma noradrenaline:0.2–0.4 ng/ml; plasma 5-HI:approx. 126 ng/ml; platelet 5-HT:(0.07 μg/2 × 10^8 platelets—one series only).

modification[12] of that used by Drummond and Gordon.[13] The catecholamine assay was a modification of the method of Causon *et al.*[14]

Discussion

This experience with ketanserin suggests that it may be an extremely useful agent for the acute control of hypertension in patients with carcinoid syndrome undergoing major procedures. Despite pre-operative preparation, cardiovascular stability is known to be difficult to maintain in some patients and considerable fluctuations in 5-HT levels have been noted in association with flushing episodes.[15] In our patient, pre-operative treatment with cyproheptadine did not prevent peroperative flushing and hypertension and oral ketanserin may be a better alternative.[10] Plasma 5-HI and platelet 5-HT levels remained high (Table 1, Fig. 1) while flushing and hypertension resolved, suggesting that 5-HT_2 receptor blockade is the mechanism of action of ketanserin. Catecholamine levels rose markedly and ketanserin could also have prevented the amplification effect of 5-HT on catecholamine-induced hypertension, or direct alpha-1-adrenoceptor blockade could have been involved. Whatever the exact mechanism of action, ketanserin appears to be a useful agent in the perioperative management of the carcinoid syndrome.

Acknowledgment

Ketanserin was supplied by Janssen Pharmaceuticals Ltd.

References

1. Wenting GJ, Man in 't Veld AJ, Woittiez AJ, Boomsma F, Schalekamp MADH. Treatment of hypertension with ketanserin, a new selective 5-HT_2 receptor antagonist. *British Medical Journal* 1982; **284:** 537–9.
2. De Cree J, Verhaegen H, Symoens J. Acute blood-pressure-lowering effect of ketanserin. *Lancet* 1981; **1:** 1161–2.
3. Editorial. Ketanserin: a selective serotonin antagonist. *Lancet* 1982; **2:** 859.
4. Millar JA, Facoory BD, Laverty R. Mechanism of action of ketanserin. *Lancet* 1982; **2:** 1154.
5. Hedner T, Persson B, Berglund G. Experience with ketanserin, a serotonin (S_2) antagonist, in longterm treatment of essential hypertension. *Clinical and Experimental Hypertension*. Part A, Theory and Practice. 1984; **6:** 743–51.
6. Van Nueten JM, Leysen JE, Schuurkes JAJ, Vanhoutte PM. Ketanserin: a selective antagonist of 5-HT_2 serotoninergic receptors. *Lancet* 1983; **1:** 297–8.
7. Vermylen J, Fiocchi R, Fagard R, Lijnen P, Staessen J, Amery A. Alpha antagonistic and

antiserotoninergic action during administration of ketanserin. *British Medical Journal* 1983; **287:** 1551–2.

8. Marwood JF, Stokes GS. Studies on the mechanism of action of the hypotensive effect of ketanserin. *Clinical and Experimental Pharmacology and Physiology* 1984; **111:** 125–32.
9. McCall RB, Schuette MR. Evidence for an alpha-1 receptor-mediated central sympathoinhibitory action of ketanserin. *Journal of Pharmacology and Experimental Therapeutics* 1984; **228:** 704–10.
10. Fischler M, Dentan M, Westerman MN, Vourc'h G, Freitag B. Prophylactic use of ketanserin in a patient with carcinoid syndrome. *British Journal of Anaesthesia* 1983; **55:** 920.
11. Maton PN, Camilleri M, Griffin G, Allison DJ, Hodgson HJF, Chadwick VS. Role of hepatic arterial embolisation in the carcinoid syndrome. *British Medical Journal* 1983; **287:** 932–5.
12. Anger C, Prys-Roberts C. Plasma serotonin concentrations during and after cardiac surgery. *European Journal of Anaesthesiology* 1984; **1:** 11–20.
13. Drummond AH, Gordon JL. Rapid sensitive microassay for platelet 5HT. *Thrombosis et Diathesis Haemorrhagica* 1974; **31:** 366–7.
14. Causon RC, Carruthers ME, Rodright R. Assay of plasma catecholamine by liquid chromatography with electrochemical detector. *Analytical Biochemistry* 1981; **116:** 223.
15. Törnebrandt K, Nobin A, Ericsson M, Thomson D. Circulation, respiration and serotonin levels in carcinoid patients during neurolept anaesthesia. *Anaesthesia* 1983; **38:** 957–67.

Anaesthesia, 1986, Volume 41, pages 600–604

CASE REPORT

Anaphylaxis to precurarising doses of gallamine triethiodide

J. F. HARRISON AND A. G. BIRD

Summary

Two cases are described in which patients developed acute anaphylactic reactions to precurarising doses of gallamine. Life threatening complications can arise from the use of small doses of drugs as adjuncts to anaesthesia and raises the question whether the benefits of precurarisation outweigh the risks of anaphylaxis.

Key words

Neuromuscular relaxants; gallamine.
Allergy; anaphylaxis.

Gallamine hypersensitivity has been well documented. Early reports in the United Kingdom from Lopert[1] and Walmsley[2] described cutaneous flushing after its use. This was followed in the early seventies, by several reports of bronchospasm during anaesthesia in which gallamine had been used,[3-6] but, despite skin testing, gallamine was not conclusively proved to be the cause. Since then, only two cases have been reported in the British literature, from Brown 1978[7] and Harrison 1981,[8] in which although gallamine was used as part of an induction sequence, no positive identification of the causative agent was obtained on either occasion.

In Australia, however, there have been several reports in recent years from Evans,[9] McKie,[10] Fisher[11] (three cases) and Long[12] (four cases), all identifying gallamine as the causative drug on subsequent skin testing. Furthermore, in a review of skin testing from the Immunology Department in Auckland, New Zealand,[13] 54 suspected cases of gallamine hypersensitivity were investigated, with fifteen positive results, in a period from 1977–1983.

This apparent geographical difference has been commented on by Fisher,[11] and it has been suggested that previous exposure to unknown environmental compounds could sensitise the patient to the quaternary ammonium group found in muscle relaxants. Alternatively, the differences could simply be a reflection of usage, or even a failure by British anaesthetists to report reactions.

Gallamine hypersensitivity has been well reported, but anaphylaxis to precurarising doses is relatively uncommon. Brown[7] described a case where gallamine was suspected as the culprit, but this could not be confirmed from skin testing, and in a recent review of intradermal testing from Wellington, New Zealand,[14] only three cases of anaphylaxis to precurarising doses of unspecified relaxants were cited over a 7-year period.

The two cases described below occurred in a 5-month period in the Newcastle area, and tend to

---

J.F. Harrison, MB, BS, FFARCS, Registrar, Department of Anaesthetics, A.G. Bird, MD, MRCP, MRCPath, Consultant Immunologist, Newcastle General Hospital, Westgate Road, Newcastle upon Tyne, NE4 6BE.

0003–2409/86/060600 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

suggest that adverse reactions to gallamine are perhaps more common than previously realised.

Case histories

Case one

A 23-year-old woman with insulin-dependent diabetes was admitted for extraction of wisdom teeth. She had undergone three previous operations for cataract surgery without incident; anaesthesia was conducted using thiopentone and suxamethonium with halothane as maintenance on each occasion. No history of atopy or allergy was obtained pre-operatively. A glucose/insulin/potassium infusion was in progress and blood sugar was 7–10 mmol/litre before induction.

Gallamine 20 mg, fentanyl 40 μg and lignocaine 1% 1 ml to reduce the discomfort of subsequent methohexitone were mixed in the same syringe and injected intravenously as a bolus. Almost immediately the patient complained of a constricting sensation in her throat, began to cough and requested that the procedure be terminated. Methohexitone 100 mg and suxamethonium 75 mg were given intravenously and a nasal tracheal tube was passed. The patient then became very pale, sweaty, intensely vasoconstricted and peripherally cyanosed and although her radial pulse was impalpable and blood pressure unrecordable, a carotid pulse could be felt.

An electrocardiograph showed a sinus tachycardia of 150 beats/minute; the patient was ventilated with 100% oxygen and an infusion of normal saline was commenced. One litre of normal saline was given over 10 minutes, her systolic blood pressure rose to 70 mmHg, the cyanosis disappeared and she began breathing spontaneously.

On return of consciousness the patient was extubated and transferred to the intensive care unit, where the systolic blood pressure was 50 mmHg, heart rate 120 beats/minute and blood sugar 10 mmol/litre. Six hours later the patient developed finger and facial oedema with a diffusely flushed appearance over her arms and trunk. This subsided over the next 24 hours, her blood pressure returned to pre-operative values and she was later discharged home. Blood was taken for IgE, C_3, C_4 and total haemolytic complement (CH_{50}) on days 1, 2 and 7, and showed an initial reduction in C_4 and CH_{50} compatible with an anaphylactic reaction and a slight rise in IgE (Table 1). Eight weeks later, intradermal testing for all the agents used was undertaken and showed no reaction to any of them except gallamine at a dose of 4 μg which produced an immediate dermal reaction with a 2.5 cm diameter wheal at 10 minutes, associated with a feeling of throat constriction lasting 2 minutes. Three months following the incident, she was admitted for wisdom teeth extraction and received an uneventful anaesthetic consisting of a gaseous induction and intubation using halothane, nitrous oxide and oxygen.

Case two

A 54-year-old woman with a past history of hypertension treated with oxprenolol and methyldopa was admitted for bilateral antral washouts. In the past she had undergone a hernia repair as a child and antral washouts 18 months previously, receiving an uneventful anaesthetic consisting of thiopentone and suxamethonium with nitrous oxide, oxygen and halothane as maintenance. She admitted to a penicillin allergy on questioning.

A precurarising dose of gallamine 18 mg was followed by induction of anaesthesia with methohexitone 55 mg with 0.8 ml lignocaine 1% during which she began to cough and jerk her head. The trachea was intubated after suxamethonium 75 mg and immediately afterwards the patient became cyanosed with a markedly raised inflation pressure suggestive of bronchospasm. The carotid pulse was impalpable, so external cardiac massage was commenced, the patient ventilated with 100% oxygen and terbutaline 0.5 mg, hydrocortisone 200 mg and

Table 1. Immunological investigations

	C_3 (0.75–1.5 g/litre)			C_4 (0.14–0.42 g/litre)			CH_{50} (1260–2880 g/litre)	IgE (10–150 i.u.)	
	1 hour	24 hours	7 days	1 hour	24 hours	7 days	1 hour	1 hour	3/12
Case 1	0.83	0.85	0.99	0.14	0.16	0.19	800	170	236
Case 2	0.91	0.81	0.96	0.18	0.15	0.19	1600	36	?

Table 2. Intradermal skin tests

Drug	Case 1	Case 2
Lignocaine	Negative	Negative
Fentanyl	Negative	(Not done)
Gallamine	4 μg strongly positive	2 μg strongly positive
Suxamethonium	500 μg weak positive	250 μg weak positive
Methohexitone	Negative	Negative

chlorpheniramine 10 mg given intravenously to reverse the bronchospasm. Five minutes later the patient's colour improved, with relaxation of the bronchospasm and return of the carotid pulse. She began breathing spontaneously, consciousness returned and her skin became a diffuse salmon-pink.

One hour later the patient was transferred to the intensive care unit at the base hospital five miles distant, where she was found to be alert and responsive, with a systolic blood pressure of 100 mmHg and a heart rate of 140 beats/minute. After a further hour, she was extubated without incident and 6 hours later her blood pressure and pulse had returned to pre-operative values.

Immunological investigations undertaken on days 1, 2 and 7 were all within normal limits (Table 1), but skin testing after 6 weeks revealed a marked wheal and flare to gallamine after a 2 μg intradermal injection, with no response to any other drug used, (Table 2).

Discussion

Mechanism of anaphylaxis

Neuromuscular blocking agents possess the ability to cause histamine release[15] and, according to one viewpoint, reactions to them may be due to an unexplained increase in mast cell sensitivity.[13] This would explain cross-sensitivity between similar drugs and first exposure reactions, but not their low incidence or relationship with atopy.

More recent evidence would suggest an IgE-mediated mechanism in a proportion of cases, based on immediate intradermal skin sensitivity, after single drug challenge with concentrations far below that necessary for histamine release in normal subjects,[13,16,17] and from the use of radio-allergo-sorption techniques (RAST) to detect specific IgE antibodies to drugs in the sera of reactors.

In this report we have not fully established the mechanism responsible for the observed reactions to gallamine. However, the extreme sensitivity of both subjects to intradermal challenge with very small doses of gallamine, associated with the relative insensitivity to suxamethonium challenge does not support direct histamine release as an explanation in these cases. At the doses of gallamine used for intradermal challenge, no positive reactions have been described in normal control subjects or individuals who received prior uneventful anaesthesia[13,18] and limited personal observations in control subjects confirm this experience. In these two patients, positive intradermal challenge tests to gallamine were obtained with doses of the drug that are only explicable by specific sensitivity of mast cells to that agent. Whether such sensitivity reflects mast cell idiosyncrasy, or IgE-arming would require further investigation.

The technique of radio-allergo-sorption for detecting drug-specific IgE antibodies has not only lent credence to the suggestion that environmental compounds, e.g. cosmetics, may cause previous sensitisation to relaxant drugs by the detection of specific IgE antibodies in the sera of patients without previous drug exposure,[19] but has also revealed considerable cross-reactivity of IgE antibodies between different relaxants, perhaps directed against the common quaternary ammonium group.[19] This latter fact, when considered in combination with the work from Youngman,[13] who skin tested 13 cases of suxamethonium sensitivity and found ten positive to both gallamine and tubocurarine, and five to alcuronium, would suggest that clinical cross-sensitivity between relaxants is a definite entity, and therefore should be borne in mind when known reactors to relaxant drugs receive subsequent anaesthesia.

Management

Treatment should be aimed at restoring intravascular volume by the rapid infusion of one or two litres of colloid or crystalloid, securing the airway with a tracheal tube and ventilation with oxygen. The presence of bronchospasm demands the use of bronchodilator drugs, but the use of adrenaline, so often advocated in acute anaphylaxis, is less certain and in both the cases reported it was considered inappropriate in the presence of tachycardias in excess of 150 beats/minute and the appearance of intense vasoconstriction.

Following initial resuscitation, transfer to an intensive care unit is essential and blood testing for IgE, RAST and complement assays undertaken on days 1, 2 and 7; the patient should be then referred for skin testing at a regional immunological centre after 6 weeks.

After identification of the causative agent, the patient should be advised to wear a 'medic alert' bracelet.

Alternative agents for precurarisation

The benefits of precurarisation were investigated by Foster[20] and White[21] in the early sixties. Foster found a reduction from 59 percent to 38 percent in the incidence of muscle pains following suxamethonium, in outpatients pretreated with gallamine 20 mg, while White showed a similar reduction in a population undergoing bronchoscopy. Clearly, this is a distinct advantage in the day case or minor surgery patient, but does the added risk of anaphylaxis outweigh any advantage gained by its use?

On present evidence, at least in the United Kingdom, the incidence of gallamine anaphylaxis is apparently so low that little benefit would ensue from avoiding its use, especially as the outcome of cardiovascular collapse is invariably good; on the other hand, any reduction in the incidence of anaphylaxis under anaesthesia must improve its safety, and from the immunologists view point, a reduction in the number of agents used during anaesthetic induction would greatly simplify the elucidation of clinical problems when they do occur.

In an effort to find a more suitable drug for the prevention of suxamethonium pains, it would appear that neither alcuronium, pancuronium, nor tubocurarine have anything to offer as alternatives, since in a review by Clarke[22] of reported anaphylactic reactions, gallamine produced 17, tubocurarine 13, alcuronium seven and pancuronium five.

The recent introduction of vecuronium, with its rapid onset of action and absence of pharmacological side effects, initially suggested a low potential for anaphylaxis and promised to be an ideal agent for pretreatment. However, there has already been at least one report of a serious anaphylactic reaction following its use.[23] It therefore remains to be seen whether it will have any advantage over the other non-depolarising agents, by possessing a significantly lower incidence of anaphylactic reactions.

Conclusions

Rapid anaphylaxis can follow the use of small doses of gallamine for precurarisation. In view of this, the role of gallamine administered in precurarising doses before suxamethonium should be re-assessed. The suggestion of an abnormal response to a drug during an anaesthetic induction sequence should prompt its termination and not, as happened in the first case, be ignored, since in retrospect the addition of methohexitone undoubtedly compounded the cardiovascular collapse and complicated the immunological investigation. The evidence of cross-reactivity between relaxants seems to imply that a patient reacting adversely to one relaxant should only receive subsequent relaxants under careful supervision.

Acknowledgments

We wish to thank Professor C.J. Hull for his advice and encouragement and Mrs Sherley Tordoss and Mrs Gena Simpson for secretarial assistance.

References

1. LOPERT H. Allergic reaction to gallamine triethiodide. *Anaesthesia* 1955; **10:** 76–7.
2. WALMSLEY DA. Sensitivity reactions to gallamine triethiodide. *Lancet* 1959; **2:** 237–8.
3. SNIPER HA. Anaphylaxis under anaesthesia. *Anaesthesia* 1971; **26:** 527.
4. HOLMES RP, ROSS JW, WILLIAMS ER. Acute anaphylaxis under anaesthesia. *Anaesthesia* 1971; **26:** 363–7.
5. WATT HK. Anaphylactic shock from gallamine. *New Zealand Society of Anaesthetists Newsletter* 1973; **20:** 21.
6. OKAZAKI K, SAITO T, WAKISAKA K, HIRANO T, KOZU K, OKAZAKI N. Bronchospasm possibly due to gallamine. A case report. *Tokushima Journal of Experimental Medicine* 1969; **16:** 9–14.

7. Brown DT. Allergy to gallamine, thiopentone and suxamethonium. *Anaesthesia* 1978; **33:** 666.
8. Harrison GR, Thompson ID. Adverse reaction to methohexitone and gallamine. *Anaesthesia* 1981; **36:** 40–4.
9. Evans PJD, McKinnon I. An anaphylactoid reaction to gallamine triethiodide. *Anaesthesia and Intensive Care* 1977; **5:** 239–43.
10. McKie BD. Anaphylactic reactions to gallamine. *Anaesthesia and Intensive Care* 1978; **6:** 266–7.
11. Fisher MM. Anaphylactic reactions to gallamine triethiodide. *Anaesthesia and Intensive Care* 1978; **6:** 62–5.
12. Long GT. Reactions to gallamine. *Anaesthesia and Intensive Care* 1979; **7:** 191–2.
13. Youngman PR, Taylor KM, Wilson JD. Anaphylactoid reactions to neuromuscular blocking agents: a commonly undiagnosed condition? *Lancet* 1983; **2:** 597–9.
14. Galletly DC, Treuren BC. Anaphylactoid reactions during anaesthesia. Seven years' experience of intradermal testing. *Anaesthesia* 1985; **40:** 329–33.
15. Beaven MA. Anaphylactoid reactions to anesthetic drugs. *Anesthesiology* 1981; **55:** 3–5.
16. Vervloet D, Arnaud A, Vellieux D, Kaplanski S, Charpin J. Anaphylactic reactions to muscle relaxants under general anesthesia. *Journal of Allergy and Clinical Immunology* 1979; **63:** 348–53.
17. Fisher MM. Intradermal testing in the diagnosis of acute anaphylaxis during anaesthesia; results of five years experience. *Anaesthesia and Intensive Care* 1979; **7:** 58–61.
18. Vervloet D, Nizankowska E, Arnaud A, Senft M, Alazia M, Charpin J. Adverse reactions to suxamethonium and other muscle relaxants under general anesthesia. *Journal of Allergy and Clinical Immunology* 1983; **71:** 552–9.
19. Baldo BA, Fisher M. Anaphylaxis to muscle relaxant drugs: cross-reactivity and molecular basis of binding of IgE antibodies detected by radioimmuno assay. *Molecular Immunology* 1983; **20:** 1393–400.
20. Foster CA. Muscle pains that follow administration of suxamethonium. *British Medical Journal* 1960; **2:** 24–5.
21. White DC. Observations on the prevention of muscle pains after suxamethonium. *British Journal of Anaesthesia* 1962; **34:** 332–5.
22. Clarke RSJ. Hypersensitivity reactions to intravenous anaesthetic drugs. In: Atkinson RS, Hewer CL, eds. *Recent advances in anaesthesia and analgesia*, No. 14. Edinburgh: Churchill Livingstone 1982: 55–79.
23. Lavery GG, Hewitt AJ, Kenny NT. Possible histamine release after vecuronium. *Anaesthesia* 1985; **40:** 389–90.

Anaesthesia, 1986, Volume 41, pages 605–610

CASE REPORT

Pulmonary occlusion (wedge) angiography in adult respiratory distress syndrome

A survey of angiographic appearances and outcomes

P. G. LAWLER

Summary

Pulmonary occlusion angiography was performed in 34 patients admitted to the intensive therapy unit with a diagnosis of adult respiratory distress syndrome. Twenty angiograms were normal. Ten patients survived. No patient with abnormal angiography survived.

Key words

Lung; adult respiratory distress syndrome.
Measurement techniques; pulmonary occlusion angiography.

Adult respiratory distress syndrome (ARDS) is a sinister component of severe illness. Tate and Repine stated that the mortality of patients suffering from ARDS exceeds 50% and that, at least in the USA, ARDS appeared to have an incidence greater than that of lung cancer.[1]

Pulmonary hypertension and a raised pulmonary vascular resistance are constant features of ARDS. A progressive fall in pulmonary vascular resistance is an indicator of survival.[2] In the normal lung, mean pulmonary artery pressure is largely independent of cardiac output and the vascular tree behaves as a Starling resistor, with the resistance falling as cardiac output rises. In ARDS, however, the pressure–flow diagram for lung vasculature suggests a significant degree of vasoconstriction or obstructive pulmonary vascular disease.[3] Furthermore, raised pulmonary vascular resistance is not simply a consequence of hypoxic pulmonary vasoconstriction[4] or a fall in lung volume. Studies on survivors of ARDS have shown a reduction in pulmonary capillary blood volume, compatible with a fall in the total pulmonary vascular area.[5] Postmortem studies of the lung vasculature of patients who have died from ARDS have shown obliteration of the alveolar–capillary bed, intra-alveolar haemorrhage, small vessel thrombi and emboli, infiltration with fibrous tissue and 'remodelling' of the vascular tree with extension of the muscular coat of the large pulmonary vessels into more peripheral vessels.[6–9]

Greene *et al.*[10] applied the technique of pulmonary occlusion (or 'wedge') angiography to patients suffering from ARDS. This allowed visualisation of the pulmonary vascular tree in critically ill patients using a method easily applicable to the intensive therapy unit (ITU). In this technique, the balloon of a pulmonary flotation catheter was inflated, the catheter wedged and radio-opaque contrast injected through the distal lumen to displace the blood filling the occluded vascular tree. A portable chest X ray then disclosed the status of the vascular tree. They studied 40 patients, of whom 18 had angiograms which were judged to be normal; the

---

P.G. Lawler, BM, MRCP, FFARCS, Consultant in Anaesthesia and Intensive Care, Intensive Therapy Unit, South Cleveland Hospital, Marton Road, Middlesbrough, Cleveland TS3 4BW.

0003–2409/86/060605 + 06 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

rest were abnormal. The survival rate in patients whose angiographic pattern was abnormal was very low.

A retrospective analysis of angiograms obtained in this ITU in the period 1 January 1983 to 31 December 1984, has been made.

Methods

Patients admitted to the ITU with a provisional diagnosis of ARDS were studied. Balloon-tipped, flow-directed pulmonary artery catheters (American Edwards) were inserted in all patients in whom the diagnosis was considered likely and in whom positive pressure ventilation was also in progress. A diagnosis of ARDS was made if the history was appropriate, the patient was hypoxic, the chest X ray showed air space consolidation (pulmonary oedema), the lung compliance was poor and the pulmonary capillary wedge pressure was less than 12 mmHg with a serum albumin concentration of over 30 g/litre. Oncotic pressure measurement was not available during this period. All patients showed pulmonary hypertension, but because cardiac output catheters were not usually inserted, calculation of pulmonary vascular resistance was not possible.

Angiography was performed immediately after insertion of the pulmonary artery catheter. Following wedging of the catheter, 15 ml sodium/meglumine ioxaglate (Hexabrix, May and Baker Ltd, Dagenham, Essex) contrast was injected through the distal lumen. The dye was injected by hand by the author as rapidly as possible. A portable chest radiograph, with the lungs held inflated at 0.3 kPa, was performed immediately following injection of contrast. Following X ray, the balloon was deflated and the catheter was flushed for 15 seconds. On no occasion was there any increase in pulmonary artery pressure following injection of contrast.

The chest X ray was reviewed and the angiographic appearance assessed immediately by the author, with particular attention to the venous filling phase, since its absence would suggest insufficient volume of contrast; however, it was always present. If the angiogram showed a filling defect in a large vessel, it was repeated immediately to ensure that this was not due to injection of an inadequate volume of contrast. On no occasion was there any change in the vascular pattern and any filling defects remained.

No ethical clearance was obtained for this study because the treatment and investigation were part of the routine management of patients suffering from ARDS.

Results

Pulmonary angiography was performed on 34 patients in the 2-year period. There were no complications and no failures. The mean age of

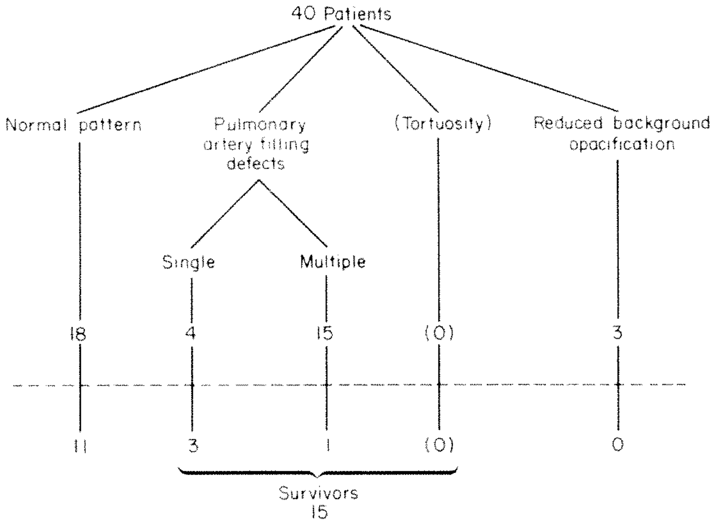


Table 1. Data from Greene *et al.*[10] to show distribution of angiographic appearances and survival in 40 patients suffering from acute respiratory failure. Note that tortuosity was not seen in this series.

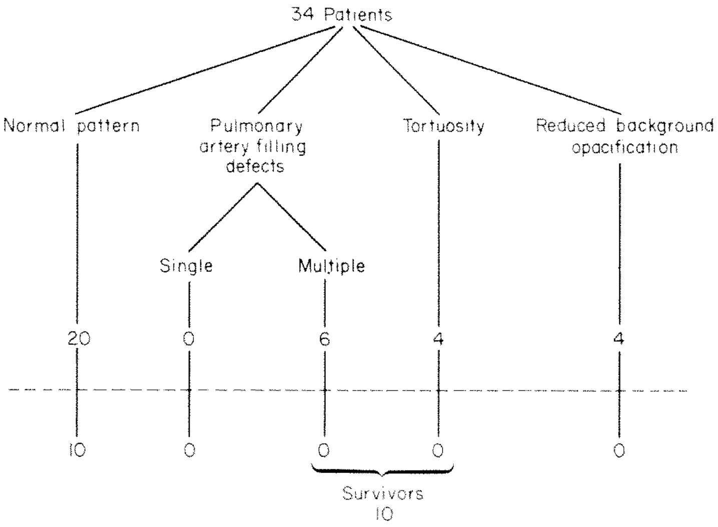


Table 2. Data of 34 patients and adult respiratory distress syndrome (ARDS), to show distribution of angiographic appearances and survival.

the patients was 53 years.

Angiograms were classified as normal or abnormal (Table 2). Abnormal angiograms were described on the basis of the predominant feature and classified as showing reduced background opacification (capillaries not seen), minor vessel occlusion (attributed to thromboses or emboli), filling defects in major vessels and tortuosity of peripheral pulmonary vasculature. Example angiograms are shown in Fig. 1–5*a*.

Twenty angiograms were normal; ten of these patients survived. Fourteen angiograms showed some abnormality. None of these patients survived. Three of the six patients with filling defects in pulmonary vessels had filling defects in major vessels, and three in minor vessels, attributed to thromboses or emboli. No angiogram showed a persistent filling defect limited to a single major vessel.

During the period of the study, the treatment for ARDS remained the same, i.e. essentially supportive. Patients received high dose steroids, ketanserin, diuretics and inotropic support (dopamine, dobutamine or both). No change in therapy was made as a direct response to angiographic pattern, although vasodilators were

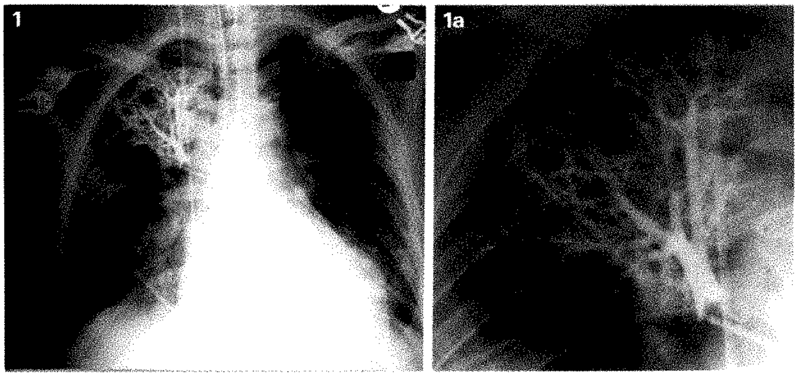


Fig. 1 and 1a. Normal pulmonary occlusion angiogram and enlarged view. The patient sustained a cardiac arrest following tamponade from a viral pericarditis. Note arterial and venous phases and multiple vessels with surrounding reticular capillary blush.

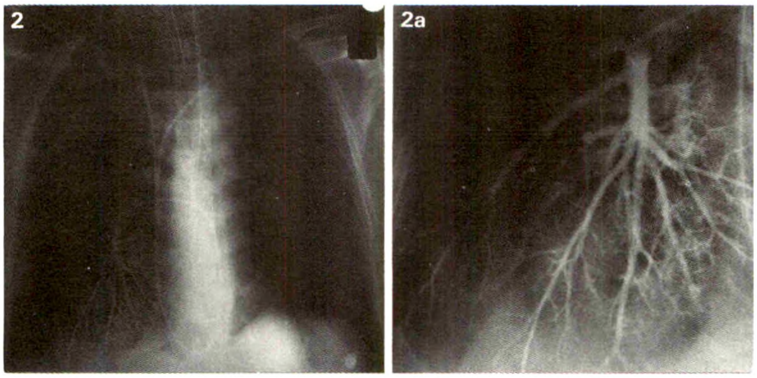


Fig. 2 and 2a. Pulmonary occlusion angiogram and enlarged view to show straightening and narrowing of vasculature, microthrombi or emboli (small filling defects) and partial loss of capillary reticular blush.

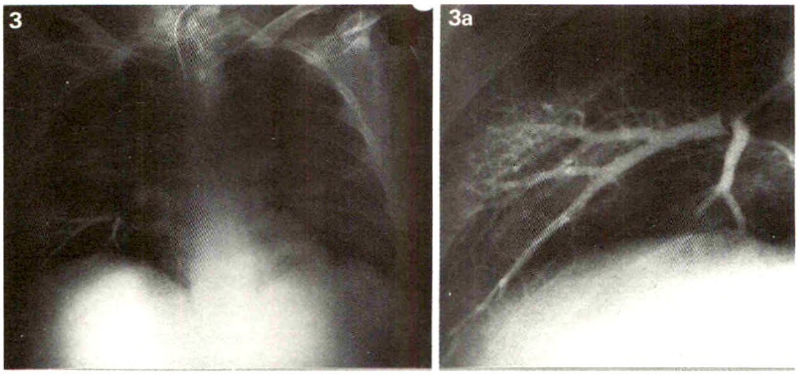


Fig. 3 and 3a. Pulmonary occlusion angiogram and enlarged view to show large vessel thromboses/emboli. These filling defects remained when the angiogram was repeated using a large volume of contrast.

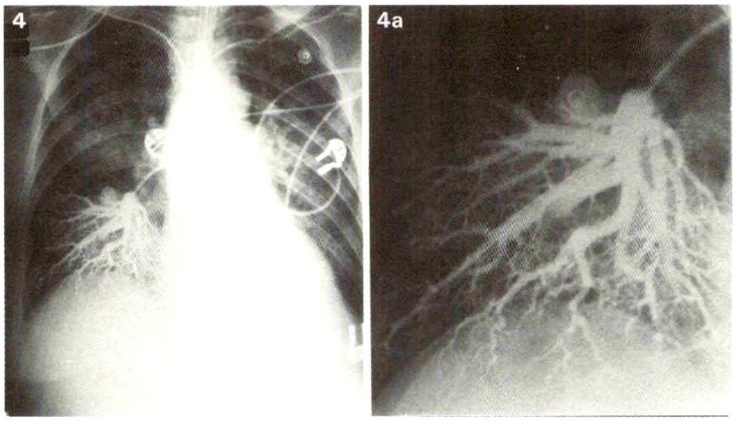


Fig. 4 and 4a. Pulmonary occlusion angiogram and enlarged view to show tortuosity of peripheral vessels. There is some loss of the capillary blush.

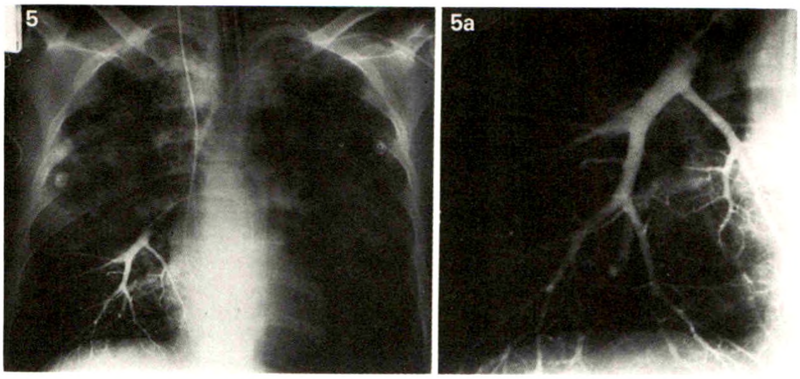


Fig. 5 and 5a. Occlusion angiogram and enlarged view showing straightening and narrowing of vessels, microthrombi/emboli and almost complete loss of capillaries (loss of background opacification).

occasionally used. Positive end expiratory pressure was used to ensure an arterial oxygen tension in excess of 10 kPa while breathing 60% oxygen. Review of patient data showed that all required positive end expiratory pressure (PEEP) oxygen tension, (0.4–1.5 kPa) all had a poly-morphonuclear neutrophilia, all were pyrexial, with positive blood cultures in over 60% of patients.

Discussion

The results of the angiographic study do not differ substantially from those reported by Greene *et al.*,[10] with a similarly dismal outlook in those patients in whom angiography showed any significant abnormality (Table 1). Our study differs in that no patient showed the single major vessel filling defects seen by Greene and colleagues; thus the outcome for these patients cannot be compared. Greene *et al.* did not comment upon patients showing a tortuosity pattern; the outlook was bad for such patients in our series. The survival rate for patients with normal angiographs was poorer in our series than that reported by Greene (50% versus 60%).

Pulmonary hypertension in patients suffering from ARDS appears to be associated with an obstructed and/or vasoconstricted pulmonary vascular tree. Abnormal angiographic patterns would appear to support these postmortem observations. The retrospective observations seen in this study are also consistent with the view that the presence of an angiographic abnormality shows that the insult leading to that abnormality has caused irreversible damage. Nevertheless, measures such as the use of vasodilators to reduce pulmonary hypertension may be appropriate: fall in pulmonary vascular resistance is associated with a better outcome.[2]

Available dilators include nitrates (e.g. glyceryl trinitrate), calcium antagonists (e.g. nifedipine),[11,12] sodium nitroprusside, alpha blockers (e.g. tolazoline) and prostacyclin. Almitrine may have a special role in vasodilating well ventilated alveoli, without overcoming hypoxic pulmonary vasoconstriction in underventilated alveoli.[13] In those patients in whom a severe obstructive element appears to be present (e.g. angiographic loss of capillaries), the role of anticoagulants or thrombolytic agents (streptokinase[14]) has not yet been clearly defined. Furthermore, because right heart failure seems likely in a proportion of these patients, the use of vasodilators is reasonable. Whether the use of vasodilators alters the outcome in these severely ill patients is currently unclear. However, a single patient, recently treated with the calcium antagonist nifedipine, has survived despite having abnormal angiography.

References

1. Tate RM, Repine JE. Neutrophils and the adult respiratory distress syndrome. *American Review of Respiratory Disease* 1983; **128:** 552–9.
2. Zapol WM, Snider MT. Pulmonary hypertension in severe acute respiratory failure. *New England Journal of Medicine* 1977; **296:** 476–80.
3. Zapol WM, Trelstad RL, Snider MT, Pontoppidan H, Lemaire F. Pathophysiologic pathways of the adult respiratory distress syndrome. In: Tinker J, Rapin M, eds. *Care of the critically ill patient.* Berlin: Springer Verlag. 1983, 341–58.
4. Snider MT, Rie MA, Lauer J, Zapol WM.

Normoxic pulmonary vasoconstriction in ARDS: detection by sodium nitroprusside (N) and isoproterenol (I) infusions. *American Review of Respiratory Disease* 1980; **121:** 191.

5. Buchser E, Leuenberger P, Chiolero R, Perret C, Freeman J. Reduced pulmonary capillary blood volume as a long-term sequel of ARDS. *Chest* 1985; **87:** 608–11.
6. Zapol WM, Kobayashi K, Snider MT, Greene R, Laver MB. Vascular obstruction causes pulmonary hypertension in severe acute respiratory failure. *Chest* 1977; **71:** 306–7 (Supplement 2).
7. Pinet F, Tabib A, Clermont A, Loire R, Motin J, Artru F. Posttraumatic-shock lung: postmortem microangiographic and pathologic correlation. *American Journal of Roentgenology* 1982; **139:** 449–54.
8. Snow RL, Davies P, Pontoppidan H, Zapol WM, Reid L. Pulmonary vascular remodeling in adult respiratory distress syndrome. *American Review of Respiratory Disease* 1982; **126:** 887–92.
9. Bachofen M, Weibel ER. Alterations of the gas exchange apparatus in adult respiratory insufficiency associated with septicemia. *American Review of Respiratory Disease* 1977; **116:** 589–615.
10. Greene R, Zapol WM, Snider MT, Reid L, Snow R, O'Connell RS, Novelline RA. Early bedside detection of pulmonary vascular occlusion during acute respiratory failure. *American Review of Respiratory Disease* 1981; **124:** 593–601.
11. Simonneau G, Escourrou P, Duroux P, Lockhart A. Inhibition of hypoxic pulmonary vasoconstriction by nifedipine. *New England Journal of Medicine* 1981; **304:** 1582–5.
12. Michael JR, Kennedy TP, Fitzpatrick S, Rosenstein BJ. Nifedipine inhibits hypoxic pulmonary vasoconstriction during rest and exercise in patients with cystic fibrosis and cor pulmonale. *American Review of Respiratory Disease* 1984; **130:** 516–9.
13. Romaldini H, Rodriguez-Roisin R, Wagner PD, West JB. Enhancement of hypoxic pulmonary vasoconstriction by almitrine in the dog. *American Review of Respiratory Disease* 1983; **128:** 288–93.
14. Greene R, Lind S, Jantsch H, Wilson R, Jones R, Carvalho A, Reid L, Zapol W. Angiographic alterations during thrombolytic treatment of severe pulmonary vascular obstruction in the adult respiratory distress syndrome. *American Review of Respiratory Disease* 1985; **131:** A142.

Anaesthesia, 1986, Volume 41, pages 611–613

CASE REPORT

Halothane hepatitis in an 11-month-old child

R. H. WHITBURN AND E. SUMNER

Summary

Halothane hepatitis is extremely rare in childhood. However, this occurred in an 11-month-old infant, following multiple exposure to halothane. The diagnosis was confirmed by detection of specific antibodies to halothane-sensitised rabbit hepatocytes. The anaesthetic technique for a subsequent procedure with a halothane-free breathing system is also outlined.

Key words

Anaesthesia; paediatric.
Complications; hepatitis.

Halothane-associated hepatitis is a recognised complication of adult anaesthesia. However, in paediatric practice it is regarded as virtually non-existent. Lewis and Blair[1] described a case in 1982 in a 4-year-old girl who developed severe hepatitis following repeated exposure to halothane. We present our experience of an 11-month-old child who developed severe jaundice and liver disease after his seventh exposure to halothane.

Case history

The patient was an Asian male infant born with oesophageal atresia and a tracheo-oesophageal fistula (TOF). He was referred to the Hospital for Sick Children, Great Ormond Street, for treatment. He had the TOF repaired and a primary anastomosis of the oesophagus was performed on his first day of life and halothane was used as part of the anaesthetic. His initial postoperative recovery was uneventful and he was discharged home after 5 weeks.

The ensuing 12 months were complicated by recurrence of the fistula with aspiration, recurrent chest infections and difficulty in feeding. He consequently required surgery for further repair of the TOF when 15 weeks old, repeat oesophagoscopy and bronchoscopy at 22 and 36 weeks respectively, aortopexy at 37 weeks and jejunostomy at 38 weeks of age. During each of the procedures he was exposed to halothane. He developed a low grade postoperative pyrexia on all but one occasion; 38.8°C was the highest recorded temperature on any occasion. Full blood examinations performed after each operation did not show significant eosinophilia.

Eventually, the child required a third repair of recurrent TOF when 42 weeks old, thus subjecting him to his seventh halothane anaesthetic. During the procedure the child received a blood

---

R.H. Whitburn*, MB, BS, FFARCS, Registrar, E. Sumner, BM, BCh, FFARCS, Consultant Anaesthetist, The Hospital for Sick Children, Great Ormond Street, London WC1N 3JH.

*Present address: Department of Anaesthetics, Alfred Hospital, Commercial Road, Prahran, Victoria, Australia.

0003–2409/86/060611 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

transfusion of 50 ml. However, at no time intraoperatively or postoperatively was there a recorded period of hypotension. He was ventilated electively after the operation and there were no reported episodes of hypoxia. On the first and second postoperative days, the child spiked a temperature of 40.0°C. He was also noted to have a tachycardia and had 1.5 cm of palpable hepatomegaly. On the fourth day he became jaundiced with a predominantly conjugated hyperbilirubinaemia. His liver function tests were as follows: serum bilirubin 163 μmol/litre (conjugated bilirubin 142 μmol/litre), alanine aminotransferase (ALT) 1890 units/litre, alkaline phosphatase (ALP) 818 units/litre, prothrombin time 34 seconds (control 13 seconds), partial thromboplastin time kaolin 65 seconds (control 34 seconds), thrombin time 25 seconds (control 10 seconds). There was an eosinophilia of 8%. A screen for sepsis, which included blood and urine cultures, was negative as were tests for infectious and serum hepatitis. Halothane hepatitis was eventually suspected and serum was sent to the King's College Hospital for detection of specific antibodies directed against the surface of halothane-altered rabbit hepatocytes. Surprisingly, the result was positive. Subsequently, the child's liver function deteriorated marginally but he soon made progress to a full recovery and liver function tests returned to normal 10 days after the onset of jaundice.

Three months later, the child presented again for surgery, for a Nissen's fundoplication. The anaesthetic technique used included a halothane-free system with cylinders of oxygen and air, flowmeters and clear polyvinyl chloride tubing was used to deliver a fresh gas flow, into a halothane-free T-piece system. Anaesthesia was induced with intravenous thiopentone, followed by suxamethonium; intubation was performed with a disposable tracheal tube (Portex). Anaesthesia was maintained with fentanyl, tubocurarine, a small dose of diazepam and manual ventilation with a mixture of oxygen and air. Neuromuscular block was reversed at the end of the procedure with neostigmine and atropine and the child was extubated. His postoperative course was uneventful, although he did develop a low grade pyrexia which subsequently resolved. Interestingly, on the third day after operation there was an eosinophil count of 10%. However, the child did not develop jaundice and made an otherwise uncomplicated recovery.

Discussion

Halothane hepatitis in children is rare. Wark in 1983[2] reviewed the incidence of postoperative jaundice at the Hospital for Sick Children, Great Ormond Street, during a 23-year period between 1957 and 1979. In this survey, he concluded that the risk of a child becoming jaundiced due to halothane-associated hepatitis was less than 1:82 000. This compares with the incidence of the disease in adult patients of between 1:6000 and 1:22 000[3]. The reason for this discrepancy in the incidence remains to be elucidated.

There are two possible mechanisms involved in the pathogenesis of halothane-associated hepatitis.[4] First, reactive metabolites of halothane, produced as a consequence of enhanced liver metabolism by either oxidative or reductive pathways, bind to liver cell macromolecules, causing enzyme inactivation and lipid peroxidation. This may, in turn, interfere with the normal production of the surface membrane, thus rendering it immunogenic. Second, the halothane molecule itself may act as a hapten and by directly reacting in some way with the cell membrane, may produce antigenicity and consequently an appropriate lymphocyte reaction against the hepatocyte.

Unfortunately, neither of these theories of the possible mechanism of halothane hepatotoxicity lends any explanation to the relative rarity of the disease in children compared to adults; nor do they enable one to predict at what age the adult incidence occurs. The possibility of a limited ability in children to metabolise halothane by the reductive pathway has been discounted by the identification of reductive metabolites in the exhaled breath of children receiving halothane.[5] Furthermore, as immune competence is present from birth, children should theoretically demonstrate similar behaviour to adults in response to the drug.[2] It has been suggested that children may have a resistance to liver damage induced by halothane metabolites due to the presence of protective substances such as free radical scavengers, or, alternatively, that their livers have a greater capacity to recover from insult than their adult counterparts.[5] The patient's family lives in Bangladesh and the family history has not been elucidated.

Our patient developed halothane-associated hepatitis on this seventh exposure to the agent, possibly because of progressive sensitisation to

Table 1. Some causes of postoperative jaundice, after Sabiston[6]

Haemolysis
Operative stress superimposed on pre-existing liver disease
Liver hypoxia during operation—hypoxaemia or underperfusion
Leakage of bile into peritoneal cavity
Viral hepatitis
Drug or anaesthetic toxicity
Extrahepatic biliary tract disorder
Hepatic infection with abscess
Septicaemia
Pulmonary embolism

halothane or increasing hepatic enzyme induction with each successive anaesthetic. Despite its rarity, halothane hepatitis should be considered a possibility in the list (Table 1)[6] of differential diagnoses of postoperative jaundice. The diagnosis may be difficult to make, but clinical criteria which should arouse suspicion include: repeated exposure to halothane within a short period of time, onset of high pyrexia and jaundice postoperatively, severe liver injury confirmed by grossly abnormal prothrombin time, eosinophilia of greater than 7% and exclusion of other causes of postoperative liver damage.[7] However, eosinophilia is a nonspecific hypersensitivity reaction and its occurrence postoperatively is of doubtful significance.

It would appear at present, that the best diagnostic indicator is the presence of circulating antibodies reacting specifically with the cell membrane of hepatocytes isolated from halothane-exposed rabbits.[8] These antibodies were first detected by Vergani *et al.*,[9] who showed that the antibodies are only detectable in patients with halothane-induced fulminant hepatic failure and were not present after repeated occupational exposure to the drug, after an uncomplicated halothane anaesthetic or during any other acute liver disease.[8] Neuberger *et al.*[10] propose that the presence of halothane-related antibody is a diagnostic test for halothane hepatitis, based on experience of 16 patients with liver damage after exposure to anaesthetic doses of the drug. On the basis of the presence of antibody, it is possible to distinguish those patients with halothane-related liver failure from those with viral or other types of hepatitis.

In conclusion, we still regard the repeated use of halothane in children as safe anaesthetic practice. However, we do recommend that the diagnosis of halothane hepatitis be entertained and excluded in the event of unexplained postoperative jaundice in a child repeatedly exposed to halothane. If the diagnosis cannot be excluded, then appropriate precautions should be taken to prevent further exposure and the risk of severe hepatic failure.

Acknowledgment

The help of the staff of King's College Hospital who carried out the halothane-related antibody diagnostic test is gratefully acknowledged.

References

1. Lewis RB, Blair M. Halothane hepatitis in a young child. *British Journal of Anaesthesia* 1982; **54:** 349–54.
2. Wark HJ. Postoperative jaundice in children. The influence of halothane. *Anaesthesia* 1983; **38:** 237–42.
3. Mushin WW, Rosen M, Jones EV. Post-halothane jaundice in relation to previous administration of halothane. *British Medical Journal* 1971; **3:** 18–22.
4. Neuberger J, Williams R. Halothane anaesthesia and liver damage. *British Medical Journal* 1984; **289:** 1136–9.
5. Plummer JL, Van Der Walt JH, Cousins MJ. Reductive metabolism of halothane in children. *Anaesthesia and Intensive Care* 1984; **12:** 293–5.
6. Sabiston DC, ed. *Textbook of surgery—the biological basis of modern surgical practice.* WB Saunders Company, 1977.
7. Fujiwara M, Watanabe A, Sato Y, Shiota T, Nakatsukasa H, Yamada G, Nagashima H. Clinical significance of eosinophilia in the diagnosis of halothane-induced liver injury. *Acta Medica Okayama* 1984; **38:** 35–40.
8. Vergani D, Mieli-Vergani G, Alberti A, Neuberger J, Eddleston ALWF, Davis M, Williams R. Antibodies to the surface of halothane-altered rabbit hepatocytes in patients with severe halothane-associated hepatitis. *New England Journal of Medicine* 1980; **303:** 66–71.
9. Vergani D, Mieli-Vergani G, Alberti A, Eddleston ALWF, Davis M, Williams R. Demonstration of a circulating antibody to halothane altered hepatocytes in patients with hepatitis. *Gut* 1978; **19:** A994.
10. Neuberger J, Gimson AES, Davis M, Williams R. Specific serological markers in the diagnosis of fulminant hepatic failure associated with halothane anaesthesia. *British Journal of Anaesthesia* 1983; **55:** 15–9.

Anaesthesia, 1986, Volume 41, pages 614–619

CASE REPORT

Acute rhabdomyolysis following surgery for burns

Possible role of tourniquet ischaemia

P. M. PFEIFER

Summary

A case is reported of acute rhabdomyolytic renal failure following surgery for minor superficial skin burns. Rhabdomyolysis apparently started peri-operatively. Possible initiating causes are discussed, notably tourniquet ischaemia. The pathophysiology, diagnosis and treatment are reviewed.

Key words

Complications; burns, tourniquets.
Muscle, skeletal; injury, myoglobinuria, rhabdomyolysis.

Rhabdomyolysis is an acute degenerative process which occurs in striated muscle. A number of factors can trigger this process, some of which are encountered in anaesthetic practice. The following case is reported because rhabdomyolysis is unusual following superficial skin burns and because it appeared to have been triggered peri-operatively. The case demonstrates the potential severity of the condition, its presentation and the differential diagnosis. Theories on the aetiology of rhabdomolytic renal failure and its treatment are reviewed.

Case history

A 14-year-old school boy (weight 54 kg) presented with 17% burns following contact with fat from a chip pan. The right leg had full thickness burns and there were superficial burns on the left shin, right forearm and abdomen. Prior to this he had been fit and well; he had had a Ramstedt's operation for pyloric stenosis at 9 months of age, was on no medication and had no known allergies.

On admission he was alert and orientated, not shocked, only mildly distressed and there was no respiratory problem. Cardiovascular observations, full blood count, serum electrolytes and blood gases were all normal.

Three days later he presented for skin grafting of his lower limbs and the pre-operative anaesthetic assessment was unremarkable. Following oral premedication of 10 mg temazepam, anaesthesia was induced with fentanyl 150 μg, thiopentone 300 mg and alcuronium 15 mg. A small dose of glycopyronium (0.2 mg) was given after induction, to dry secretions. Following tracheal intubation, anaesthesia was maintained by intermittent positive pressure ventilation of the lungs with 30% oxygen in nitrous oxide and further supplements of fentanyl 125 μg and alcuronium 10 mg. Enflurane 0.5% was used intermittently, amounting to 25% of the total 3-hour anaesthetic.

P.M. Pfeifer, PhD, FFARCS, Senior Registrar, Department of Anaesthetics, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP.

0003–2409/86/060614 + 06 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

A tourniquet, inflated to a pressure of 520 mmHg, was applied high up on the right thigh for 45 minutes. Despite a respiratory minute volume of 8 litres/minute, he remained normocapnoeic with an end tidal carbon dioxide ($P\text{E}'\text{CO}_2$) of 4.5 to 4.7 kPa, attributed to the hypermetabolic state that can accompany burns, until the release of the tourniquet when the $P\text{E}'\text{CO}_2$ rose to 5.5 kPa. Peri-operatively, the patient received 500 ml dextrose/saline and four units of whole blood. The blood pressure and pulse were stable at approximately 130/80 mmHg throughout the operation. Muscle relaxant reversal was achieved with glycopyronium 0.4 mg and neostigmine 2.5 mg. The postoperative visit 20 minutes later revealed a fully alert, non-distressed patient with stable observations and on direct questioning he admitted only to a mild burning sensation in his feet.

Five hours postoperatively he became distressed, tachypnoeic (25 breaths/minute), hypotensive (100/60mmHg) and pyrexial at 38°C. Investigations revealed a serum potassium of 8.6 mmol/litre, sodium 128 mmol/litre and bicarbonate 15 mmol/litre. The serum urea and creatinine were slightly elevated at 8.8 mmol/litre and 179 μmol/litre respectively. The haemoglobin was 13.9 g/dlitre and the white cell count was 21.7×10^9/litre. Arterial blood gas analysis showed pH 7.19, arterial oxygen tension ($P\text{aO}_2$) 6.7 kPa (spontaneous ventilation in air), arterial carbon dioxide tension ($P\text{aCO}_2$) 6.2 kPa and a base deficit of -10.5 mmol/litre. Chest X ray, blood glucose and clotting screen were normal. The differential diagnosis at this stage was recorded as either septicaemia, a blood transfusion reaction or an anaesthetic reaction.

He was initially treated with calcium gluconate (20 ml of 10% solution), dextrose/insulin infusion, sodium bicarbonate (100 ml of 8.4% solution), methylprednisolone 2 gm, catheterised and transferred to the intensive care unit. On admission he was given 35% oxygen and a further 40 ml of 10% calcium gluconate and 50 ml of 8.4% sodium bicarbonate. Blood cultures were taken and triple antibiotic therapy was started with ampicillin, gentamycin and metronidazole. Arterial and central venous pressure lines were inserted. The central venous pressure was $+5$ cmH$_2$O. Further blood tests taken at this time later revealed a creatine phosphokinase (CPK) level of greater than 2000 units (normal up to 175) and a lactate dehydrogenase of 7965 units (normal up to 430).

Overnight he produced only 300 ml of very dark brown urine and remained oliguric despite treatment with increasing doses of frusemide to a maximum dose of 1 g. Two days later his serum urea and creatinine were 25.6 mmol/litre and 497 μmol/litre respectively and peritoneal dialysis was started for treatment of his acute renal failure.

The increased serum potassium was controlled at approximately 6 mmol/litre with dextrose/insulin. He was dialysed for 17 days, during which time the serum calcium underwent significant changes as shown in Fig. 1. Immediately after the operation, total serum calcium dropped to 1.48 mmol/litre (normal is 2.12–2.62 mmol/litre) and an infusion of 10% calcium gluconate was commenced at 10 ml/hour and continued for approximately 48 hours. After 5 days the serum calcium reached normal levels and by 8 days it had reached 2.97 mmol/litre. The hypercalcaemia was not treated and the level declined into the normal range by day 9.

Further investigations revealed no growth in blood and urine cultures, suggesting that sepsis was not the cause of the acute renal failure. A blood transfusion reaction was not the cause since the crossmatch was rechecked and found to be compatible; the patient had normal haptoglobin and bilirubin levels and a normal reticulocyte count. An electrophoretic test on the early postoperative urine to determine the identity of the chromagen (haemoglobin or myoglobin) was not performed due to microbial contamination and growth in the stored specimen.

This may have been a mild aborted form of malignant hyperpyrexia so a deltoid muscle biopsy was taken under local anaesthesia. However, histology revealed normal muscle fibres with numerous randomly distributed areas of active muscle fibre necrosis, phagocytosis and regeneration. It was a monophasic insult as all the areas of degeneration were at the same timepoint in the pathological process. The most impressive histological features were scattered large areas, usually within muscle fibres, of haematoxophilic material, which was shown to be calcium. There was a predominance of type 1 fibres and the small regenerating fibres were all of the type 2C in profile. This histology, together with the relatively slow onset of clinical features and absence of rigidity suggested the diagnosis of toxic rhabdomyolysis.

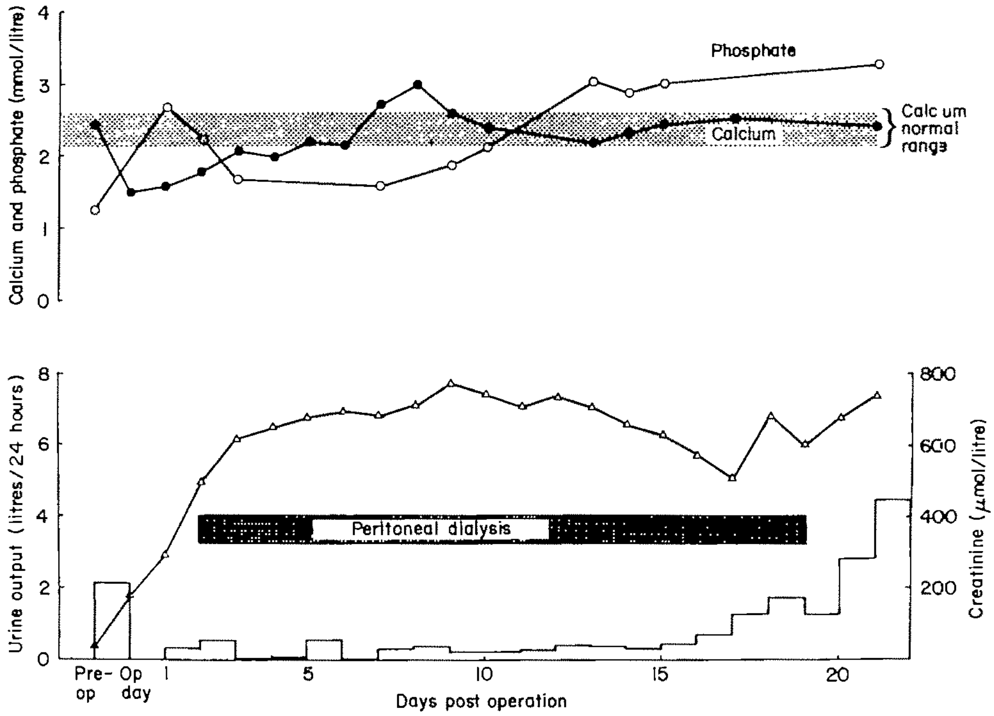


Fig. 1. Serum concentrations of calcium, phosphate and creatinine and daily urine volumes during the course of acute rhabdomyolytic renal failure following surgery for superficial skin burns. ●—●, calcium; ○—○, phosphate; △—△, creatinine.

The patient was discharged from hospital 4 weeks after the operation and followup in the outpatient department showed complete recovery.

Discussion

Rhabdomyolysis and acute renal failure following crush injuries are well recognised and were described as early as 1941 during the Battle of Britain.[1] Rhabdomyolysis without progression to renal failure has subsequently been associated with many conditions and Table 1 describes some of these.

Burns due to electrical injuries and lightning strikes are well recorded causes of rhabdomyolysis,[10-13] but rhabdomyolysis due to heat burns is not. Chugh *et al.* in 1979[11] reported a fatal case of rhabdomyolytic renal failure following a flame burn. Their patient suffered a large 70–80% burn and showed evidence of gross heat injury to muscle. In 1982, Walsh *et al.*[13] used a sensitive immunoassay procedure to measure myoglobin in the blood of 26 burned patients, 15 of whom had flame burns. Twenty-three patients had detectable myoglobinaemia which correlated with the depth of burn, but not the surface area. Seventeen of the patients had detectable myoglobinuria but 16 of the 17 had normal renal function, as demonstrated by normal serum urea, creatinine and urine output. Our case report is of a patient who developed acute rhabdomyolytic renal failure following a relatively minor 17% nonelectrical burn.

A further unusual feature of this case is the abrupt peri-operative onset. The patient had been stable for 3 days between the burn and the surgery. There appears to have been an additive or triggering muscle insult from the surgery or the anaesthetic. A direct anaesthetic cause is unlikely. There were no general hypotensive or hypoxic episodes. Suxamethonium, the cause of a recently reported case of rhabdomyolytic renal failure,[4] was not used in the only other case known to the author, in which enflurane was given to a patient who subsequently developed rhabdomyolytic renal failure. Alcuronium, fentanyl and glycopy-

Table 1. Actiologies of rhabdomyolysis (modified and compiled from references 2–13)

Trauma to normal muscle	Crush, convulsions, electroconvulsive therapy, strenuous exercise, prolonged coma, eclampsia, prolonged labour, muscle ischaemia, burns
Abnormal muscle states	Polymyositis, dermatomyositis, phosphorylase deficiency, myopathies, e.g. McArdles, Duchenne muscular dystrophy
Drugs	Alcohol, heroin, methadone, suxamethonium, barbiturates, ethylene glycol, carbenoxolone
Infection	Tetanus, gas gangrene, Coxsackie, viral influenza
Hyperthermia	Heat stroke, fever, malignant hyperpyrexia
Metabolic disturbances	Hypokalaemia, hypophosphataemia, myxoedema, sickle cell anaemia

ronium are not known to be causes of rhabdomyolysis. Our patient did receive thiopentone. Rhabdomyolysis due to barbiturates is most probably not a direct result of the drug itself, but rather a consequence of hypotension and ischaemia following drug induced coma.[14] Indeed, barbiturates have been shown to have a protective effect against suxamethonium induced release of CPK.[15]

Skin grafting is unlikely to damage muscle since it is superficial surgery. The tourniquet, however, *does* produce muscle ischaemia and this may be more significant in the hypercatabolic state that can accompany burns. Rhabdomyolysis following a tourniquet is rare. The report by Williams *et al.*[2] followed the application of a mid-thigh tourniquet for 2 hours 14 minutes; the tourniquet was released for 13 minutes, and then re-inflated for a further 2 hours 7 minutes—a relatively long tourniquet time. The maximum safe tourniquet time can not be calculated; it is a clinical judgement, based on the patient's condition, considering factors such as the degree of vascular disease and the amount of surgical time required. Our patient had a tourniquet time of only 45 minutes, but even this may have contributed to the subsequent development of rhabdomyolysis. It may be that muscle insults such as burns and ischaemia are additive. It should be noted that it is not just the absolute tourniquet time that is relevant, there is the 'no reflow phenomenon' described by Strock and Majno.[16] They studied carbon black infusions following tourniquet-induced rat limb muscle ischaemia and showed that blood flow did not immediately return to normal even after short ischaemic periods, e.g. 15 minutes.

If muscle insults are additive, anaesthetists should be aware of the other known causes of rhabdomyolysis shown in Table 1, because many of these conditions may be present in patients who present for anaesthesia. The diagnosis and treatment of rhabdomyolysis and the prevention of renal failure follow from an understanding of the pathophysiology. Trauma causes necrosis of the muscle cell. Phagocytosis and regeneration may occur if the area is not totally damaged or avascular. Myoglobin, potassium and creatinine are released into the circulation. Creatinine is a cyclic degradation product of phosphocreatine which is an energy storage compound in striated and cardiac muscle. Phosphocreatine is formed by ATP-driven phosphorylation of creatine, catalysed by the enzyme creatinine phosphokinase (CPK). In rhabdomyolysis, the sudden release of relatively large amounts of creatinine from within the muscle cells cause the characteristic rapid rise in serum creatinine, often in the order of 0.2 mmol/litre/day.[4] This rapid rise is out of proportion to the rise in serum urea. The enzyme CPK is also released in vast amounts.

The release of free phosphate causes a fall in serum calcium due to the deposition of calcium phosphate salts in the injured muscle. These were clearly seen in the histological slides from our patient. Consideration of this mechanism of the cause of the hypocalcaemia would suggest that it should not be treated by calcium infusion unless there are clinical problems such as dysrhythmias or hypotension. The later hypercalcaemia may be associated with elevated levels of 1,25-dihydroxy cholecalciferol,[17] or increased urinary phosphate secretion due to an elevated parathyroid hormone level.[18]

A number of possible causes of the onset of renal failure have been postulated.[2] Pigmented casts have been seen in the renal tubules of biopsy specimens and these have been shown to be plugs of precipitated myoglobin, which could cause obstructive damage.[19] In acid urine, pH <5.6, myoglobin dissociates into ferrihaemate and globin and it has been suggested that ferrihaemate is toxic to the tubular epithelium, allowing back diffusion to occur.[20] Another suggested mechanism is a decreased glomerular permeability due to deposition of fibrin. Electron microscope pictures of fibrin strands in human renal cortex following myoglobinuric renal failure have been demonstrated.[21] Renal ischaemia may be potentiated by alterations of the renin-angiotensin and sympathetic nervous systems, thus causing oliguric renal failure.[22]

The diagnosis of rhabdomyolysis is suggested by the raised serum CPK and the raised creatinine that is out of proportion to the serum urea. The presence of myoglobin in the urine is pathognomonic. Myoglobin gives a positive result with the o-toluidine test for occult urinary blood. Myoglobin is a single haem-containing protein with a molecular weight of 16 000 and may be differentiated from haemoglobin by gel electrophoresis, immunodiffusion or column chromatography.[2,23] The hypo-, and subsequent hyper-calcaemia is also characteristic of rhabdomyolysis. Clinical symptoms and signs are of muscle pain and oedema, oliguria with dark urine, hypotension and possibly dysrhythmias.

Treatment is based on the concept that the pathophysiology described above would be worsened by hypovolaemia, acidosis and hypotension. A recommended regimen[24] includes infusions of mannitol and bicarbonate and aggressive correction of hypovolaemia with careful monitoring of urine output. If the urine output increases, then the infusion rate should be maintained. If, however, after a few hours oliguria persists, or anuria develops, then fluid restriction and treatment for established renal failure should be instituted. There may be large fluid shifts in the early stage into the damaged muscle areas and central venous pressure monitoring may be required. Serum electrolytes, dysrhythmias, respiratory failure and pain should be managed according to standard medical practice. It has been suggested that the hypocalcaemia should not be treated.[4] The hypercalcaemia has been postulated to occur in the diuretic phase, due to the urinary secretion of phosphate thus allowing the reabsorption of the deposited calcium salts. In this case, the hypercalcaemia occurred while the patient was still oliguric. This may be a result of the removal of phosphate by peritoneal dialysis. Thus, it may be possible to treat a dangerous hypercalcaemia by manipulation of the phosphate content of the dialysing fluid.

Rhabdomyolysis, which can progress to life-threatening renal failure, is a relatively uncommon condition. The case presented is unusual as it followed a relatively minor nonelectrical burn. The use of a tourniquet in this case may have been an additive insult to muscle that initiated the rhabdomyolysis. Some of the predisposing conditions to rhabdomyolysis are found in patients presenting for surgery, so anaesthetists should be aware of the condition and of its treatment in the intensive care unit.

References

1. Bywaters EGL, Beall D. Crush injuries with impairment of renal function. *British Medical Journal* 1941; **1:** 427–32.
2. Williams JE Jr, Tucker DB, Read JM. Rhabdomyolysis–myoglobinurea: consequences of prolonged tourniquet. *Journal of Foot Surgery* 1983; **22:** 52–6.
3. Grossman RA, Hamilton RW, Morse BM, Penn AS, Goldberg M. Non traumatic rhabdomyolysis and acute renal failure. *New England Journal of Medicine* 1974; **291:** 807–11.
4. Hool GJ, Lawrence PJ, Sivaneswaran N. Acute rhabdomyolytic renal failure due to suxamethonium. *Anaesthesia and Intensive Care* 1984; **12:** 360–4.
5. Devereux S, Knowles SM. Rhabdomyolysis and acute renal failure in sickle cell anaemia. *British Medical Journal* 1985; **290:** 1707.
6. Chagnac A, Rudniki C, Zevin D, Braslavsky D, Zahavi I, Levi J. The morphological changes in acute renal failure due to rhabdomyolysis following viral infection. *Nephron* 1982; **32:** 75–7.
7. El Nahas AM, Farrington K, Quyyumi S, Moorhead JF, Sweny P. Rhabdomyolysis and systemic infection. *British Medical Journal* 1983; **286:** 349–50.
8. Vertel RM, Knochel JP. Acute renal failure due to heat injury. An analysis of ten cases associated with a high incidence of myoglobinuria. *American Journal of Medicine* 1967; **43:** 435–51.
9. Selzer ML, Reinhart MJ, Deeney JM. Acute renal failure following EST. *American Journal of Psychiatry* 1963; **120:** 602–3.
10. Warden GD, Saffle JR, Kenfield K, Kravitz M. The use of plasma exchange in thermally injured patients not responding to conventional burn management. *Journal of Burn Care and Rehabilitation* 1983; **4:** 264–70.
11. Chugh KS, Singhal PC, Nath IVS, Pareek SK, Ubroi HS, Sarkar AK. Acute renal failure due to non-traumatic rhabdomyolysis. *Postgraduate*

Medical Journal 1979; **55:** 386–92.

12. Yost JW, Holmes FF. Myoglobinuria following lightning stroke. *Journal of the American Medical Association* 1974; **228:** 1147–8.
13. Walsh MB, Miller SL, Kagen LJ. Myoglobinemia in severely burned patients: correlations with severity and survival. *Journal of Trauma* 1982; **22:** 6–10.
14. Penn AS, Rowland LP, Fraser DW. Drugs, coma and myoglobinuria. *Archives of Neurology* 1972; **26:** 336–43.
15. Innes RKR, Stromme JH. Rise in serum creatine phosphokinase associated with agents used in anaesthesia. *British Journal of Anaesthesia* 1973; **45:** 185–90.
16. Strock PE, Majno G. Vascular responses to experimental tourniquet ischaemia. *Surgery of Gynecology and Obstetrics* 1969; **129:** 309–18.
17. Llach F, Felsenfeld AJ, Haussler MR. The pathophysiology of altered calcium metabolism in rhabdomyolysis-induced acute renal failure. *New England Journal of Medicine* 1981; **305:** 117–23.
18. Leonard CD, Eichner ER. Acute renal failure and transient hypercalcemia in idiopathic rhabdomyolysis. *Journal of the American Medical Association* 1970; **211:** 1539–40.
19. Kagen LJ. Immunofluorescent demonstration of myoglobin in the kidney: case report and review of forty-three cases of myoglobinemia and myoglobinuria identified immunologically. *American Journal of Medicine* 1970; **48:** 649–53.
20. Braun SR, Weiss FR, Keller AI, Ciccone JR, Preuss HG. Evaluation of the renal toxicity of heme proteins and their derivatives: a role in the genesis of acute tubule necrosis. *Journal of Experimental Medicine* 1970; **131:** 443–60.
21. Clarkson AR, MacDonald MK, Fuster V, Cash JD, Robson JS. Glomerular coagulation in acute ischaemic renal failure. *Quarterly Journal of Medicine* 1970; **39:** 585–99.
22. Ellis D, Gartner JC, Galvis AG. Acute renal failure in infants and children: diagnosis, complications, and treatment. *Critical Care Medicine* 1981; **9:** 607–17.
23. Markowitz H, Wobig GH. Quantitative method for estimating myoglobin in urine. *Clinical Chemistry* 1977; **23:** 1689–93.
24. Eneas JF, Schoenfeld PY, Humphreys MH. The effect of infusion of mannitol-sodium bicarbonate on the clinical course of myoglobinuria. *Archives of Internal Medicine* 1979; **139:** 801–5.

Anaesthesia, 1986, Volume 41, pages 620–622

CASE REPORT

Intensive care aspects of severe *Legionella* pneumonia

K.J. POWER AND D.J. BOWEN

Summary

A case of extensive Legionella pneumonia is presented. The patient required an extended period of artificial ventilation, notably punctuated by episodes of dysrhythmia and severe haemodynamic instability, but who nevertheless eventually recovered. Intensive care aspects of Legionnaires' disease are discussed.

Key words

Legionnaires' disease.

Case history

A previously healthy, 64-year-old man presented with a 6-day history of a 'flu-like' illness, associated with increasing dyspnoea. Over the 2 days prior to admission, he became increasingly confused. On examination he was cyanosed, febrile (39°C) and tachypnoeic (50 breaths/minute). He had a tachycardia of 140 beats/minute and a blood pressure of 90/60 mmHg. Examination of the chest revealed poor air entry bilaterally, associated with bronchospasm and widespread crepitations.

Initial blood gases were taken with the patient receiving oxygen therapy with an MC mask at an oxygen flow of 8 litres/minute. They confirmed severe hypoxia; $P\text{a}O_2$ 6.9 kPa, $P\text{a}CO_2$ 4.09 kPa, pH 7.32, HCO_3 15.7 mmol/litre. Chest X ray demonstrated an extensive bilateral pneumonia. (Fig. 1). Elective ventilation of the lungs was undertaken. An $F\text{I}O_2$ of 0.6 and positive end expiratory pressure (PEEP, 0.5 kPa) were

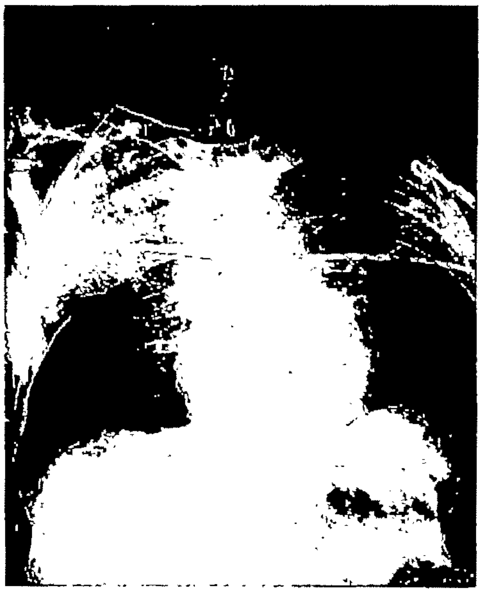


Fig. 1. Chest X ray showing bilateral pneumonia.

K.J. Power MRCP, Registrar, D.J. Bowen FFARCS, Consultant, Department of Anaesthetics, Royal Hampshire County Hospital, Romsey Road, Winchester.

Correspondence should be addressed to: Dr K.J. Power, Department of Anaesthetics, Frenchay Hospital, Bristol BS16 1LE please.

0003–2409/86/060620 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

required to achieve a $Pa\text{O}_2$ of 7 kPa.

In view of the broad differential diagnosis at this stage, he was treated with broad spectrum antibiotics, with the inclusion of erythromycin to cover atypical pneumonias and Legionnaires' disease. After 5 days, a positive titre was obtained for *Legionella pneumophilia*, at which time rifampicin 300 mg twice daily was added to erythromycin 1g four times a day.

Complications

The most striking feature of this case was the occurrence of episodes of spontaneous tachycardia, associated with severe haemodynamic upset. At the initial stage of his disease, this might readily be explained in terms of the severe systemic upset. However, several further episodes of supraventricular tachycardia occurred in a total of 50 days artificial ventilation. No obvious precipitant cause could be found for these episodes. There was no arterial hypoxaemia at any stage, electrolytes were normal and there was no evidence of pulmonary embolus or myocardial infarction. This raises the possibility of a direct involvement of the myocardium in the infective process. Although this has previously been reported,[1] it is not widely recognised as a common complication. Pericardial involvement has also been reported.[2]

A total of 50 days artificial ventilation was required before adequate blood gases could be achieved by spontaneous ventilation. Throughout this period, the patient was in an extremely catabolic state, which required initially parenteral and later enteral nutrition.

Discussion

Although only first recognised as a specific entity in 1976, Legionnaires' disease is now increasingly recognised as a common cause of pneumonia. Indeed, it has been estimated that 12% of all pneumonias requiring hospital admission may be due to *Legionella*.[3] The disease process itself is thought to be due to the synergistic activity of more than one toxin produced by this gram negative bacillus.[4]

Outbreaks tend to occur in institutions and have a predilection for elderly male smokers and particularly for subjects with any depression of cell-mediated immunity.[5] The spectrum of disease following *Legionella* infection is broad, ranging from the mild Pontiac fever[6] which was first described in 1968, and is associated with general malaise, myalgia and a low grade fever, through to an overwhelming pneumonia with systemic organ involvement.[7] The disease is particularly aggressive in patients with underlying malignancy and those who are immunosuppressed following organ transplantation.[5] The pneumonic process itself is particularly severe in subjects with pre-existing abnormalities of lung function.[5]

Person to person transmission does not occur[4] and the patient does not require strict isolation. In view of this, staff in contact with patients do not require special surveillance. Should an outbreak occur in hospital, the efforts of the public health department are directed towards ascertaining the source that has become contaminated with the organism. Likely sources include water traps and air conditioning systems. The disease is not notifiable.

The disease process chiefly involves the terminal bronchioles and alveoli leading to pneumonic consolidation. Pleural effusions occur in severe cases, but rarely proceed to frank empyema.[4] Clinically, prodromal symptoms are succeeded by increasing dyspnoea, cough, pleuritic pain and haemoptysis. Ninety-five % of patients are febrile[4] and 65% of patients have a relative bradycardia.[7] Radiologically extensive consolidation may occur, although cavitation is unusual. A deterioration in the X ray appearance may suggest the occurrence of a superadded infection; however, it is recognised that a radiological deterioration may occur despite clinical improvement.[4]

Laboratory findings indicate the multisystem nature of the disease. Hyponatraemia and hypophosphataemia are frequent.[7] Elevated serum transaminases may reflect liver damage. However, rifampicin therapy used in the treatment of severe cases will itself cause a rise in the hepatic transaminases. Leucocytosis is common, but leucopaenia and thrombocytopaenia may both occur, although only the former is associated with a poor prognosis.[8] Severe anaemia and disseminated intravascular coagulation are relatively rare (10% of cases).[7]

The diagnosis in this case was established by confirming a rising antibody titre to *Legionella pneumophilia* in the patient's serum. The case illustrates the importance of serial sampling as the initial antibody titre was negative, became weakly positive with a titre of 1:128 at 6 days and only rose to 1:256 on day 14. Isolated titres of 1:128 have been found in healthy individuals, which suggests the occurrence of subclinical infections leading to seroconversion. This stresses the importance of establishing a rising antibody titre in order to diagnose an acute infection, although it may take 6–8 weeks to occur, and only permits a retrospective diagnosis.[5] It is thus essential to commence the appropriate antibiotic therapy if the diagnosis is suspected on clinical grounds.

In general, direct culture of the organism is rarely attempted, although it is possible in specialist laboratories, using highly selective media. In severely immunocompromised patients in whom the differential diagnosis of a pneumonia includes such pathogenic entities as fungi and *Pneumocystis* as well as *Legionella*, direct culture might be worthwhile in attempting to establish a definite diagnosis. This will require aspiration of secretions at fibre-optic bronchoscopy or open lung biopsy. In the latter case, a rapid diagnosis can be made using a direct fluorescent antibody technique. It is relevant to note that samples of bacteria obtained by bronchoscopy may be inhibited by the use of topical lignocaine.[4]

As illustrated here, severe cases may require prolonged periods of cardiovascular and respiratory support. Steroid therapy, however, has been associated with a higher mortality rate, due to its immunosuppressive action. Mortality in severe cases associated with immunosuppression may approach 60%.[7] The overall mortality rate is 15–20%.[4]

Renal failure occurs in 10% of patients and adversely influences the prognosis. Several factors probably operate in its development. Severely ill patients are often hypotensive and dehydrated, leading to prerenal oliguria and susceptibility to renal insults. Granular casts and features of glomerulonephritis have been recorded.[9] Myoglobinuria and DIC occurring in severe cases will also contribute to the development of acute renal failure.[10] In general, if recovery from the disease itself occurs, renal function should return to normal.[10]

Erythromycin in high dosage remains the drug of choice,[11] and with the increasing recognition of Legionnaires' disease and other atypical pneumonias it should always be included in the treatment of undiagnosed pneumonias. It should be given for at least 3 weeks, in a dose of 4 g daily in divided doses. *In vitro* sensitivity of the organism to penicillins and cephalosporins is not reflected by a clinical response to these agents.

The use of rifampicin (up to 1200 mg/day) may attenuate the course of severe cases. The addition of rifampicin is reserved for those cases which fail to respond to erythromycin, although in the critically ill, moribund patient, treatment with both drugs might possibly be commenced from the outset.

The recovery period may be prolonged for those who survive and may be characterised by a residual neurological deficit in cases with CNS involvement. A restrictive defect in pulmonary function may persist.[12]

Acknowledgment

The authors thank Mrs B.A. Burgess for her secretarial assistance.

References

1. Gross D, Willens H, Zeldis SM. Myocarditis in Legionnaires' disease. *Chest* 1981; **79:** 232–4.
2. Durand S, Damecour C, Jacotot B. Une observation de legionellose avec atteinte péricardique. *Presse Medicale* 1984; **13:** 1516.
3. Davis GS, Winn WCJ, Beaty HN. Legionnaires' disease. Infections caused by *Legionella pneumophilia* and *Legionella*-like organisms. *Clinical Chest Medicine* 1981; **2:** 145–66.
4. Edelstein PH, Meyer RD. Legionnaires' disease. A review. *Chest* 1984; **85:** 114–20.
5. Swartz MN. Clinical aspects of Legionnaires' disease. *Annals of Internal Medicine* 1979; **90:** 492–5.
6. Eickhoff TC. Epidemiology of Legionnaires' disease. *Annals of Internal Medicine* 1979; **90:** 499–502.
7. Francke E. Legionnaires' disease. *Postgraduate Medicine* 1983; **73:** 347–51.
8. Meyer RD. *Legionella* infections: a review of five years of research. *Review of Infectious Diseases* 1983; **5:** 258–78.
9. Saleh F, Rodichok LD, Satya-Murtis S, Tillotson JR. Legionnaires' disease—Report of a case with unusual manifestations. *Archives of Internal Medicine* 1980; **140:** 1514–6.
10. Woodhead MA, Macfarlane JT. The protean manifestations of Legionnaires' disease. *Journal of the Royal College of Physicians* 1985; **19:** 224–30.
11. Miller AC. Erythromycin in Legionnaires' disease—a re-appraisal. *Journal of Antimicrobial Chemotherapy* 1981; **7:** 217–22.
12. Lattimer GL, Ormolee RA. *Legionnaires' disease. Infectious diseases and antimicrobial agents*, Vol. 1 New York: Marcel Dekker Inc., 1981.

Anaesthesia, 1986, Volume 41, pages 623–627

CASE REPORT

Acute respiratory failure following lithium intoxication

A report of two cases

P. G. LAWLER AND J. R. COVE-SMITH

Summary

Two patients suffering from severe lithium poisoning (blood level > 4 mmol/litre) were treated by haemodialysis. Both patients developed delayed respiratory failure, with the characteristics of adult respiratory distress syndrome, at a time when lithium levels had fallen below 2 mmol/litre. We recommend early respiratory support in the treatment of severe lithium intoxication.

Key words

Ventilation; failure.
Pharmacology; lithium.

Lithium salts have been used for over 30 years as an adjunct to the treatment of manic depressive psychosis.[1] The therapeutic window is small and appropriate blood levels lie between 0.8 and 1.4 mmol/litre. Toxic symptoms occur when blood levels exceed 1.5 mmol/litre. These symptoms include confusion and impaired conscious level, ataxia, muscle twitching, tremor, blurred vision, convulsions, thirst, polyuria, vomiting and diarrhoea. Other toxic effects include myocardial irritability and depression. The kidneys provide the principal route of excretion of lithium. Excretion is somewhat enhanced by sodium loading, while salt depletion markedly enhances lithium retention. Lithium, itself, is nephrotoxic. Renal impairment or salt depletion reduces lithium excretion and a vicious circle of toxicity may therefore ensue; vomiting, diarrhoea and polyuria lead to dehydration, salt depletion, lithium retention and further impairment of renal function and lithium excretion.

Lithium carbonate is usually prescribed as a slow release preparation (Priadel). Continued absorption may delay falls in blood level following poisoning. Furthermore, the volume of distribution of lithium is that of the body water, so that blood levels will fall slowly during conventional treatment of toxicity (saline diuresis), or may rebound following haemodialysis, as a result of delayed diffusion from body tissues.

In the last year, we have treated two patients whose lithium levels on admission were 4.5 and 4.9 mmol/litre, respectively. Both these patients were treated by haemodialysis and both developed delayed respiratory failure, and required mechanical ventilation of the lungs at a time when blood lithium levels had fallen to less than 2 mmol/litre.

Case histories

Case 1

A 52-year-old lady, known to suffer from manic

P.G. Lawler, BM, MRCP, FFARCS, Consultant in Anaesthesia and Intensive Care, J.R. Cove-Smith, MD, FRCP, Consultant Physician and Nephrologist, Intensive Therapy Unit, South Cleveland Hospital, Marton Road, Middlesbrough, Cleveland TS4 3BW.

0003–2409/86/060623 + 05 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

depressive psychosis, was found confused and wandering about the town. Her psychosis had been treated with lithium carbonate (Priadel). Soon after admission to the psychiatric unit, her level of consciousness deteriorated and she was transferred to the medical unit. Her lithium level was found to be 4.5 mmol/litre. She was transferred to the intensive therapy unit (ITU) for haemodialysis and further care.

On admission to the ITU, she was drowsy but easily rousable. Her blood pressure was 140/80 mmHg with a pulse of 90 beats/minute. Her central venous pressure was 8 mmHg, measured from the mid-axillary line. Her electrolytes showed a sodium of 132 mmol/litre, potassium 3.2 mmol/litre, chloride 104 mmol/litre and bicarbonate 20 mmol/litre. Urea was 11.9 mmol/litre, creatinine 253 μmol/litre and albumin 26 g/litre. Her blood gases showed pH 7.27, $P\text{CO}_2$ 4.9 kPa, and base deficit 9 mmol/litre. Arterial $P\text{O}_2$ was 6.9 kPa breathing 28 percent oxygen. This rose to 11.9 kPa while breathing 60% oxygen. Her airway appeared adequate, and her chest X ray was clear.

Haemodialysis was undertaken via a left arm shunt and continued for 6 hours, during which time she remained rousable and continued to cough, although she tolerated a nasopharyngeal airway. Her pulse, blood pressure and central venous pressure remained stable. She received 3 units of plasma protein fraction during dialysis. Urine continued to flow during dialysis, although the output had deteriorated to 20 ml/hour. At the end of dialysis, the serum lithium level had fallen to 1.9 mmol/litre. The plasma electrolytes after dialysis were sodium 130 mmol/litre, potassium 3.0 mmol/litre, urea 2.5 mmol/litre, creatinine 139 μmol/litre and albumin 36 g/litre. Her arterial $P\text{O}_2$ following dialysis was 11 kPa breathing 60% oxygen.

Three hours after dialysis and one hour after a blood gas ($P\text{aO}_2$ 10 kPa), her ventilatory efforts appeared reduced, although she continued to cough. Blood gases showed a pH of 7.21, $P\text{aCO}_2$ 9.1 kPa, $P\text{aO}_2$ 4.9 kPa and base deficit 3 mmol/litre. Her trachea was intubated and her lungs ventilated. Large quantities of sputum were cleared from her bronchial tree during fibreoptic bronchoscopy. Over the next hour, her $P\text{aO}_2$ fell to 6.0 kPa while she was ventilated with 100% oxygen. She subsequently required inotropic support (dopamine) and positive end expiratory pressure (PEEP) of up to 0.9 kPa. Her chest X ray showed pulmomary oedema. Her albumin at this time was 37 g/litre, while her central venous pressure was 15 mmHg on PEEP of 0.9 kPa.

Over the succeeding 3 days, her oxygenation improved and PEEP and inotropic support were withdrawn. She required two further dialyses to cover the rebound of her lithium level. Urine flow continued and improved. Her trachea was extubated at 120 hours and she was discharged to the ward at 6 days. She was discharged from the hospital 4 days later with no apparent sequelae of lithium toxicity.

Case 2

A 27-year-old male manic depressive was treated with lithium carbonate (Priadel). He had received this therapy for over 2 years.

Two months before admission, he had developed polyuria and polydipsia, although this came to light only after admission to the ITU. He subsequently became more withdrawn and was admitted to the pyschiatric unit. Two days after his admission, his conscious level deteriorated and he developed abdominal pain and diarrhoea. He was transferred to the medical unit where he was seen to be severely dehydrated. He received 3 litres of crystalloid solution (mainly 0.9% saline) intravenously over the next 6 hours. His condition deteriorated and he became pyrexial (39.5°C). There was no further vomiting or diarrhoea. His level of consciousness deteriorated further and he was transferred to the ITU with a provisional diagnosis of septicaemia.

On admission, he was groaning but uncommunicative. He was coughing spontaneously and did not tolerate a nasopharyngeal airway. His pulse was 60/minute, arterial blood pressure 120/60 mmHg and central venous pressure was 18 mmHg, taken from the mid-axillary line. His abdomen was soft with active bowel sounds. Urine flow was less than 20 ml/hour. A serum lithium level, taken on admission to the ITU, was found to be 4.9 mmol/litre. He had received no lithium for at least 2 days.

Blood gases showed a pH of 7.31, $P\text{aCO}_2$ 3.2 kPa and base deficit 10 mmol/litre. The arterial $P\text{O}_2$ was 6.2 kPa breathing air, but rose to 9 kPa breathing 40% oxygen. Sodium was 142 mmol/litre, potassium 5.0 mmol/litre, chloride 108 mmol/litre and bicarbonate 18 mmol/litre. Urea was 25.2 mmol/litre creatinine 735 μmol/

litre and albumin 38 g/litre. The chest radiograph showed pulmonary oedema and the electrocardiograph showed bizarre complexes attributable to lithium toxicity.

Haemodialysis was undertaken via a single needle in the right subclavian vein. He was diafiltered initially to a venous pressure of 8 mmHg. Blood pressure (120/70 mmHg) and pulse (60–80 minute) remained stable. Arterial Po_2 rose to 11 kPa. He continued to move around the bed restlessly and to cough. He did not tolerate a nasopharyngeal airway. Haemodialysis was continued for 8 hours, by which time his serum lithium level had fallen to 1.6 mmol/litre. Pulse, blood pressure and central venous pressure were maintained throughout dialysis. Urine output fell to zero. Four hours later, the lithium level had rebounded to 2.4 mmol/litre and haemodialysis was recommenced.

Soon after the start of the second dialysis, his blood gas status declined. His $Paco_2$ rose to 7 kPa and arterial Po_2 fell to 6 kPa breathing 60% oxygen. His conscious level appeared unchanged. Blood pressure, pulse and venous pressure had remained stable. Electrolytes prior to his second dialysis were normal. At this time the urea was 10.3 mmol/litre, creatinine 331 μmol/litre, and albumin 38 g/litre.

His trachea was intubated and his lungs ventilated mechanically. Fibre-optic bronchoscopy showed much purulent sputum, which was sucked out. Arterial Po_2 was 10 kPa on 100% oxygen but over the next hour this fell to 6.4 kPa, despite breathing 100% oxygen. He was treated with PEEP and inotropic support (dopamine and dobutamine). Arterial Po_2 rose to 11 kPa on 60% oxygen and PEEP of 1.5 kPa. His chest X ray showed pulmonary oedema. Urine flow remained minimal. Dialysis was continued for a further 6 hours, by which time his lithium level had fallen to 0.8 mmol/litre. His CVP was maintained at 8–10 mmHg. Over the succeeding week, both his lung function and his renal function improved, although daily dialysis was required. Intermittent positive pressure ventilation (IPPV) with PEEP was required for 3 days and IPPV for a further 4 days. He was extubated at 11 days. Urine output improved in tandem with renal function, although he required two further dialyses following extubation. He was discharged from the ITU after 15 days and returned to the psychiatric unit at 20 days. On discharge, his renal function was still improving but remained abnormal, with a urea of 12.2 mmol/litre and a creatinine of 240 μmol/litre.

Discussion

Both these patients developed significant respiratory failure at a time when serum lithium levels were falling. Standard simple reference books of poisons management[2-4] place no particular emphasis upon respiratory failure, nor do they recommend early IPPV as a primary intervention in the management of severe lithium poisoning.

The time course and pattern of these patients' deterioration were remarkably similar. Both patients were initially hypoxic, but maintained their arterial Pco_2. Both subsequently developed increasing hypoxia with a rising Pco_2, this being the reason for intervention. At the time of intervention, both patients were hypoxic, had severe sputum retention, low central venous pressures and chest X rays which showed pulmonary oedema. Although the second patient may have had right heart failure on admission to the ITU (central venous pressure 18 mmHg), and could conceivably have had left heart failure at that time, his right atrial pressure at the time of his deterioration was low. Pulmonary oedema of cardiac origin seemed unlikely with a serum albumin of 38 g/litre. Oncotic pressure was not measured.

These features, and the response to treatment, make adult respiratory distress syndrome (ARDS) the likely diagnosis. Pulmonary artery catheters were not inserted in either patient, because at the time of their deterioration both patients were significantly heparinised. Both patients had evidence of sputum retention, but both were noted to be coughing spontaneously. Neither patient was deeply unconscious, although one was tolerant of a nasopharyngeal airway. Inhalation of gastric contents could not be ruled out with absolute certainty. Nevertheless, bronchoscopy had shown no evidence of gastric debris and both had received H_2-receptor antagonists (ranitidine) on admission to ITU. Inhalation as a cause of ARDS was unlikely.

Dialysis-induced hypoxia is well recognised, and correctable with oxygen, and reverts rapidly following cessation of dialysis.[5] Disagreement exists as to whether hypoxia is secondary to polymorphonuclear sequestration in the lung capillaries with complement and vasoactive peptide activation leading to either a diffusion defect[6-8] or ventilation perfusion inequalities,[7,8] or to dialysis membrane loss of CO_2 and consequent loss of CO_2-induced respiratory drive.[5,9,10] The latter possibility seems most likely and in the described cases would have disguised a rising Pa_{CO_2} due to an impaired respiratory drive. Measurement of $P_{0.1}$ (P_{100}) may be used as a means of assessing central drive. In this technique, the pressure drop at the mouth which occurs in the first 0.1 seconds (100 mseconds) following complete respiratory obstruction is used to assess drive. Following lithium ingestion, pressure drop is less than control values, suggesting that lithium may act as a central respiratory 'depressant'.[11] In these patients, the reversal of the metabolic acidosis by dialysis would have reduced respiratory drive still further, but the consequences of this reduction would have gone unobserved because of dialysis membrane loss of CO_2. Cessation of dialysis would lead to a progressive and unexpected deterioration in the blood gases. Sputum retention could reasonably be associated with poor respiratory drive.

In the reported patients, the distinction between dialysis-induced hypoxia and hypoxia due to ARDS would have been difficult to make without the presence of pulmonary artery catheters. Polymorphonuclear sequestration in the lung fields, for instance, is common to both,[6-8,12,13] as is a fall in platelet count. Complement activation occurs in both ARDS and during dialysis.[8,14] Nevertheless, hypoxia was present in both patients before dialysis and although hypocapnia is the usual finding in ARDS, hypercapnia can occur in severe ARDS. Dialysis-induced hypoxia should have reverted soon after cessation of dialysis.

No single explanation clearly accounts for the whole course of the respiratory illness. While the early picture might have been due to respiratory depression, with sputum retention, the subsequent pattern of events and response to therapy was in keeping with the adult respiratory distress syndrome. Lithium poisoning is not a recognised association.[15]

Conclusions

Our observations have led us to believe that early IPPV should be instituted in hypoxic, drowsy patients requiring haemodialysis for lithium poisoning. We also believe that pulmonary artery catheterisation is necessary to allow rational assessment of these patients and, in future, we shall insert such catheters. Our observations also lead us to believe that haemofiltration might be appropriate in order to avoid the rebound of lithium levels seen in such patients.

References

1. Baldessarini RJ. Drugs and the treatment of psychiatric disorders. In: Gilman AG, Goodman LS, Gilman A, eds. *The pharmacological basis of therapeutics.* 7th edn. New York: Macmillan Publishing Co. Inc, 1985; 387–445.
2. Vale JA, Meredith TJ (eds). *Poisoning: diagnosis and treatment.* London: Update Books, 1981.
3. Matthew H, Lawson AAH. *Treatment of common acute poisonings.* 4th edn. Edinburgh: Churchill Livingstone, 1979.
4. Seyffart G. *Poison index: dialysis and haemoperfusion in poisoning.* Bad Homberg: Fresenius-Foundation, 1979.
5. Aurigemma NM, Feldman NT, Gottlieb M, Ingram RH, Lazarus JM, Lowrie EG. Arterial oxygenation during hemodialysis. *New England Journal of Medicine* 1977; **297:** 871–3.
6. Toren M, Goffinet JA, Kaplow LS. Pulmonary bed sequestration of neutrophils during hemodialysis. *Blood* 1970; **36:** 337–40.
7. Carlon GC, Campfield PB, Goldiner PL, Turnbull AD. Hypoxemia during haemodialysis. *Critical Care Medicine* 1979; **7:** 497–9.
8. Craddock PR, Fehr J, Brigham KL, Kronenberg RS, Jacob HS. Complement and leukocyte-mediated pulmonary dysfunction in hemodialysis. *New England Journal of Medicine* 1977; **296:** 769–74.
9. Dolan MJ, Whipp BJ, Davidson WD, Weitzman RE, Wasserman K. Hypopnoea associated with acetate hemodialysis: carbon dioxide-flow-dependent ventilation. *New England Journal of Medicine* 1981; **305:** 72–5.
10. Romaldini H, Rodriguez-Roisin R, Lopez FA, Ziegler TW, Bencowitz HZ, Wagner PD. The mechanisms of arterial hypoxemia during hemodialysis. *American Review of Respiratory Disease* 1984; **129:** 780–4.
11. Weiner M, Chausow A, Wolpert E, Addington W, Szidon P. Effect of lithium on the responses to added respiratory resistances. *New England Journal of Medicine* 1983; **308:** 319–22.
12. Passamonte PM, Martinez AJ, Singh A. Pulmonary gallium concentration in the adult respiratory distress syndrome. *Chest* 1984; **85:** 828–30.
13. Powe JE, Short A, Sibbald WJ, Driedger AA. Pulmonary accumulation of polymorphonuclear leukocytes in the adult respiratory distress syndrome. *Critical Care Medicine* 1982; **10:** 712–8.
14. Hammerschmidt DE, Weaver LJ, Hudson LD, Craddock PR, Jacob HS. Association of

complement activation and elevated plasma-C5a with adult respiratory distress syndrome. *Lancet* 1980; **1:** 947–9.

15. Balk R, Bone RC. The adult respiratory distress syndrome. *The Medical Clinics of North America* 1983; **67:** 685–700.

Anaesthesia, 1986, Volume 41, pages 628–630

APPARATUS

A new double lumen tube adaptor

Use in adjustment of bronchial cuff volume and oxygenation

A. N. SIBAI AND A. BARAKA

Summary

The report describes a new double lumen tube adaptor which provides selective one lung ventilation without external clamping. It also facilitates, without disconnexion and remantling, both correct bronchial cuff inflation and continuous positive airway pressure administration using an underwater seal chest bottle. Oxygenation can be kept optimal during one lung anaesthesia by applying 1.0 kPa continuous positive airway pressure to the nonventilated lung using an oxygen flow of 1–2 litres/minute.

Key words

Equipment; connectors, tubes, bronchial.

Several double lumen tube adaptors have been designed to serve different functions during one lung anaesthesia.[1–4] This report describes a new double lumen tube adaptor, which facilitates interruption of ventilation to either lung, bronchial cuff end-point inflation[5] and continuous positive airway pressure (CPAP) administration to the nonventilated lung.[6]

Apparatus

The commercially available double lumen tube adaptor comprises a Carlen's Y-connector, joined to two swivel connectors by two plastic tubes. We have modified the adaptor by assembling two on–off valves (A and B, Fig 1) one on each side. A T-piece (T) is also provided on the side corresponding to the operated lung, between valve A and the swivel connector. The T-piece side arm is joined to a three-way stopcock (S).

One limb of the stopcock is attached to an underwater seal chest bottle, while the other limb receives oxygen from a flowmeter via a tubing, whenever CPAP administration is indicated. An aneroid manometer is installed between the stopcock and the underwater seal. The on–off valves, the T-piece and the three-way stopcock are made of copper and are joined together by short pieces of plastic tubes cut to suitable lengths. The internal diameter of the valves and the T-piece is 8 mm, while the stopcock internal diameter is 4 mm. The entire assembly weighs 150 g. The system is sterilised by ethylene oxide gas.

Functions

Selective one lung ventilation. This can be achieved readily with one of the two on–off valves (A or B), without the need for external clamping of the adaptor tubes.

Bronchial cuff titration. The adaptor is connected to the double lumen tube with the T-piece on the side corresponding to the operated

---

A.N. Sibai, MB, BCh, DA, Assistant Professor, Department of Anesthesiology, American University of Beirut Medical Center, Beirut, Lebanon, A. Baraka, DM, MD, DA, Professor and Chairman, Department of Anesthesiology, American University of Beirut Medical Center, Beirut, Lebanon.

0003–2409/86/060628 + 03 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

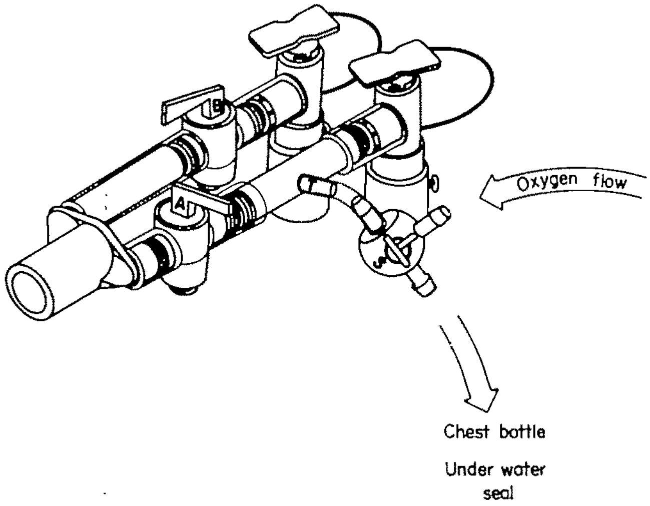


Fig. 1. The double-lumen tube adaptor: (A and B), on–off valves to interrupt ventilation to either lung. (T), T-piece assembled on the adaptor side corresponding to the operated lung. (S), a three-way stopcock connects the T-piece of the adaptor to an oxygen flowmeter and the underwater seal.

lung. After proper positioning of the double lumen tube and inflation of the tracheal cuff, the bronchial cuff volume is titrated by the following steps: valve A is off, valve B is on. The side arm of the T is opened to the chest bottle by S.

The nonoperated lung is ventilated whilst the bronchial cuff is gradually inflated: the back flow from the patient's lungs is directed through T towards the underwater seal. Bubbling continues so long as the bronchus is not sealed by the bronchial cuff; cessation of the bubbling during lung inflation indicates end point inflation of the cuff.

CPAP administration. The administration of CPAP to the operated nonventilated lung is accomplished by opening the stopcock towards its three ports, i.e. flow of oxygen, T-piece and chest bottle, while maintaining valve A off and valve B on. The oxygen passes through T and, consequently, to the nonventilated lung. The water level in the chest bottle is adjusted to provide the required CPAP, as verified by the manometer.

The technique was applied on six patients undergoing thoracotomy in the lateral position under oxygen, halothane, relaxant anaesthesia. The mean (SD) arterial oxygen tension ($P\text{ao}_2$) during two lung ventilation was 60.4 (11.55) kPa. A change to one lung ventilation reduced the $P\text{ao}_2$ to 28.88 (5.44) kPa. Application of 1.0 kPa CPAP using 1–2 litres/minute of oxygen elevated the $P\text{ao}_2$ to 57.3 kPa (SD 8).

Discussion

Correct inflation of the bronchial cuff is necessary to avoid problems and complications. Overinflation of the cuff may result in its rupture[5] or its herniation across the carina[7] and bronchial rupture has been reported.[8] Underinflation of the cuff results in cross-leak from the lower lung when one lung ventilation is initiated.[9]

In 1979, Jenkins described a technique for a visual and audible indication of a precise end point inflation of the bronchial cuff by connecting the tracheal side of the double lumen tube to an indicator bottle.[5] In our system, the underwater seal bottle is connected to the T-piece, which is an integral part of the adaptor. The bronchial cuff sealing end point can be easily checked at the beginning and during the procedure without disconnexion and remantling.

Capan *et al.*[6] reported that arterial oxygenation can be kept optimal during one lung anaesthesia by oxygen insufflation to the nonventilated lung at 1.0 kPa pressure and 7 litres/minute flow. A pressure relief valve was adjusted to maintain the required CPAP pressure.[6] Other systems for CPAP administration to the nonventilated lung during one lung anaesthesia have been devised, but none used an underwater seal.[10,11] Our system uses an underwater seal and its level is adjusted to achieve the required CPAP. The arterial $P\text{O}_2$ was markedly increased by delivering an oxygen flow as low as 1–2 litres/minute at 1.0 kPa CPAP via the T-piece of the adaptor. The CPAP administration using the underwater seal offers the advantage of stabilising the required airway pressure in the system, irrespective of the lung manipulation by the surgeon and/or increasing the oxygen flow.

References

1. Viljoen JF. A new double-lumen endobronchial tube connector. *Anesthesiology* 1967; **28:** 950–1.
2. Salt RH. A modified two-way union for double lumen tube. *Anaesthesia* 1970; **25:** 418–9.
3. Tanguturi S, Capan LM, Patel K, Turndorf H. A new double-lumen tube adaptor. *Anaesthesia and Analgesia* 1980; **59:** 507–8.
4. Anderson HW, Ozaki GT, Benumof JL. A new improved double-lumen tube adaptor. *Anesthesiology* 1982; **56:** 54–6.
5. Jenkins AV. An endobronchial cuff indicator for use in thoracic surgery. *British Journal of Anaesthesia* 1979; **51:** 905–6.
6. Capan LM, Turndorf H, Patel C, Ramanathan S, Acinapura A, Chalon J. Optimization of arterial oxygenation during one-lung anesthesia. *Anesthesia and Analgesia* 1980; **59:** 847–51.
7. Zeitlin GL, Short DH, Ryder GH. An assessment of the Robertshaw double lumen tube. *British Journal of Anaesthesia* 1965; **37:** 858–60.
8. Heiser M, Steinberg JJ, Macvaugh H. Bronchial rupture, a complication of use of the Robertshaw double-lumen tube. *Anesthesiology* 1979; **51:** 88.
9. Read RC, Friday CD, Eason CN. Prospective study of the Robertshaw endobronchial catheter in thoracic surgery. *Annals of Thoracic Surgery* 1977; **24:** 156–61.
10. Thiagarajah S, Job C, Rao A. A device for applying CPAP to the nonventilated upper lung during one lung ventilation. I. *Anesthesiology* 1984; **60:** 253–4.
11. Hannenberg AA, Satwicz PR, Dienes RS, O'Brien JC. A device for applying CPAP to the nonventilated upper lung during one lung ventilation. II. *Anesthesiology* 1984; **60:** 254–5.

Anaesthesia, 1986, Volume 41, pages 631–634

APPARATUS

No moving parts

A modification of a Bain system and a Penlon Nuffield 200 ventilator

M. N. CALHAEM

Summary

Interchange between ventilatory and spontaneously breathing modes using a Bain system and a Penlon Nuffield 200 ventilator may be achieved by the single action of switching the ventilator on or off. No alteration is made to the expiratory valve, reservoir bag, ventilator tubing or scavenging system and there are no levers.

Key words

Equipment; breathing system.
Ventilation.

The Bain system is widely used for spontaneously breathing patients[1,2] and the Bain system together with a Penlon Nuffield 200 ventilator for intermittent positive pressure ventilation.[3,4] The change of ventilatory mode requires removal of the ventilator tubing and its replacement with a reservoir bag, relocation of the scavenging system and adjustment of the expiratory valve. The apparatus described has been constructed to allow conversion from one mode to the other, merely by switching the ventilator on or off. This automatically isolates the reservoir bag and expiratory valve, yet permits the scavenging system to remain operative throughout (Fig. 1).

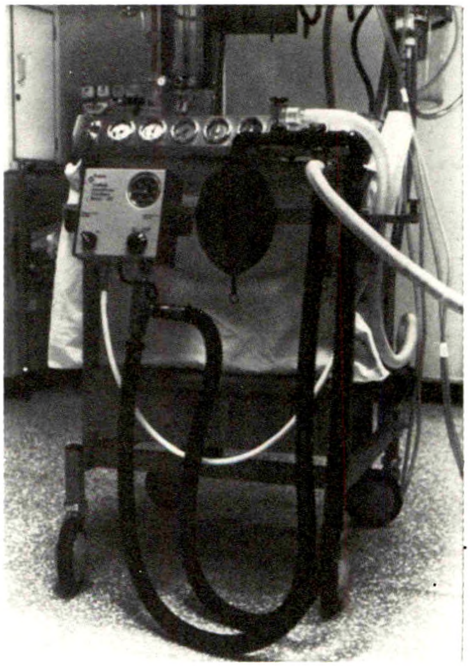


Fig. 1. The system.

Description of instrument

The expiratory adjustable pressure limiting (APL) valve was removed from the top of a Penlon Bain inlet block and replaced by a blanking plug. To this was attached (with Araldite) a plastic T-piece with one limb sawn off. This forms a support for part of the system with a reservoir bag and a modified APL valve. The system is

---

M.N. Calhaem, BSc, FFARCS, Consultant Anaesthetist, Stafford District General Hospital, Weston Road, Stafford ST16 3SA.

© 1986 The Association of Anaesthetists of Gt Britain and Ireland

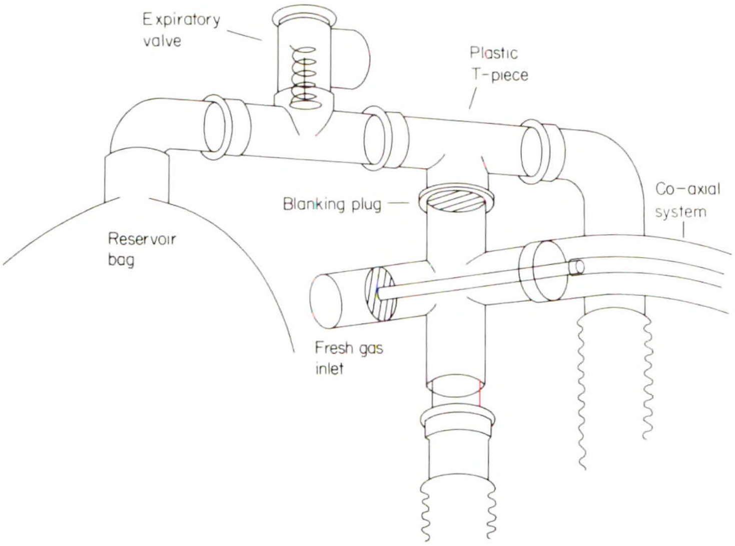


Fig. 2. Modified inlet block and expiratory valve.

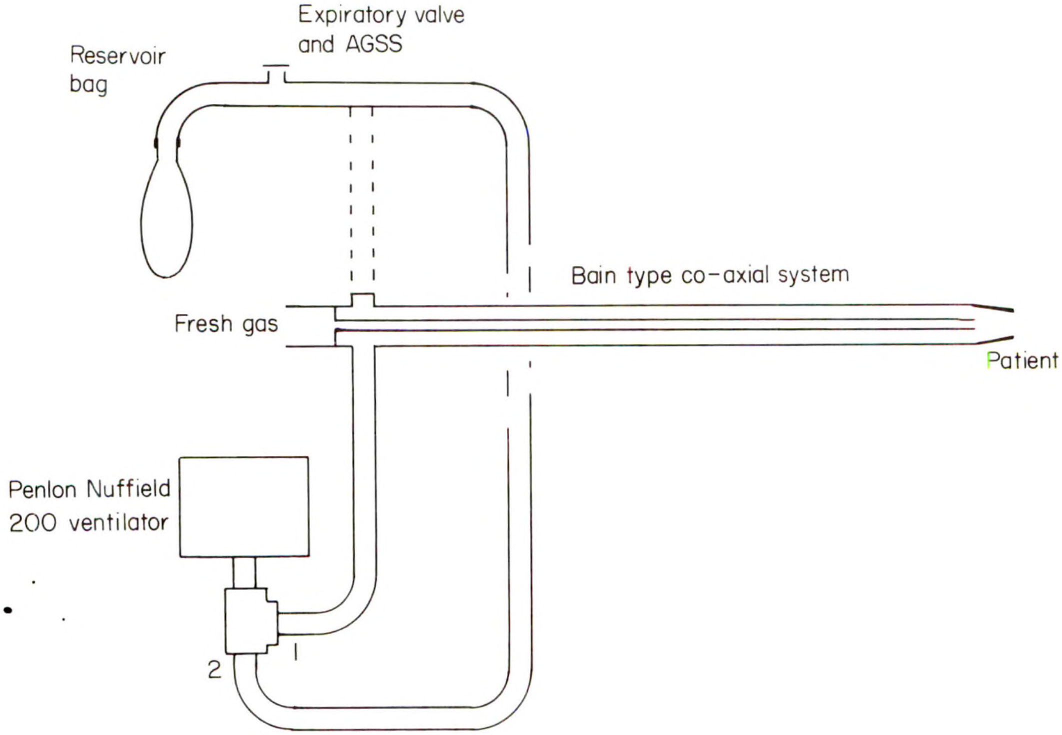

Expiratory valve and AGSS
Reservoir bag
Bain type co-axial system
Fresh gas
Patient
Penlon Nuffield 200 ventilator
1
2

Fig. 3. Diagramatic representation of the system. AGSS, anaesthetic gas scavenging system; 1, inspiratory port of patient valve; 2, expiratory port of patient valve.

shown diagramatically in Fig. 2. The APL valve is a Penlon Mk III Duct Expiratory Valve for Magill Circuit with the outer, i.e. weaker, spring removed. This means that when the valve is fully open there is no pressure on the flap, except for its own weight, yet it is still possible for the valve to be closed down for manual ventilation when the inner, stronger spring comes into play. Because the system is based on a Bain, there is a constant flow of fresh anaesthetic gas and this is sufficient to hold the reservoir bag inflated, despite the very low opening pressure of the APL valve. The reservoir bag acts only as an indicator of breathing; it does not act as a reservoir of anaesthetic gas. This gas lies entirely within the connecting tubing. If air is drawn in through the APL valve during inspiration, it is of no consequence.

Function in spontaneous mode

The patient valve of the Nuffield 200 ventilator is a simple spring loaded piston.[3] When the ventilator is inoperative the piston is held up by the spring and ports 1 and 2 (Fig. 3) are in free communication. Thus, spontaneous ventilation can occur through the patient valve, APL valve and reservoir bag, the whole performing as a Bain system.

Function in ventilatory mode

When the ventilator is switched on, the piston of the patient valve descends during the inspiratory phase and occludes port 2, thereby isolating the APL valve and reservoir bag and providing ventilation to the patient via port 1. During the expiratory phase, the piston returns to a position which permits open communication of ports 1 and 2 and expiration occurs through the patient valve and APL valve as before.

Resistance of the system

Resistance measurements were made using a simple water manometer; this was coupled to the outlets of two anaesthetic machines in series, thus achieving from the Rotameters 20 litres/minute of nitrous oxide and/or 20 litres/minute of oxygen. Thirty litres/minute of oxygen was achieved by using a special high flow oxygen. Rotameter on the outlet of one machine.

The gas was passed to the breathing system in the direction appropriate for the resistance being measured. Thus for inspiratory resistance, the flow was passed from the port for the reservoir bag to the patient connexion; the APL valve was closed. For expiratory resistance, the flow was passed from the patient connexion to the anaes-

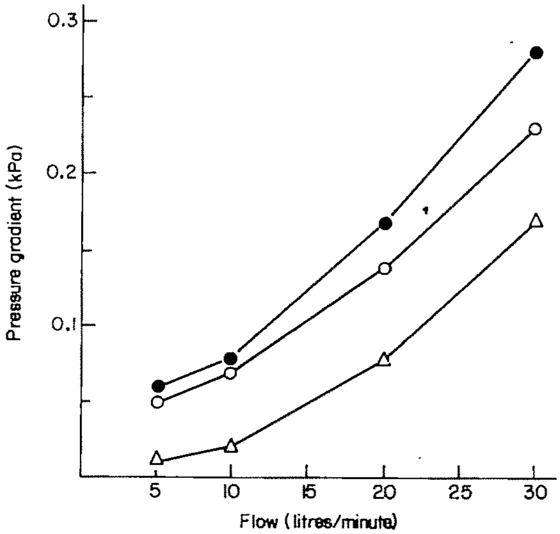


Fig. 4. Resistance of the system. ▲—▲, inspiratory resistance with 50% N_2O/O_2; ●—●, expiratory resistance with 50% N_2O/O_2; ○—○, expiratory resistance with 100% O_2.

thetic gas scavenging system; the APL valve was fully open, the reservoir bag in place and the gas inlet port sealed.

Pressure measurements were made at various flows and gas mixtures and the results are shown in Fig. 4. These resistances are well within the acceptable limits stated by Nunn.[5] These values are further ameliorated by the reservoir bag cushioning the expiratory resistance.

Discussion

The device succeeds in producing a system that switches between spontaneous and ventilatory modes by a single action, i.e. switching on or off the ventilator. The single action is convenient, safe, cheap and easy to construct. The APL valve and reservoir bag are in a convenient place for hand and eye and the system does not offer undue resistance to inspiratory and expiratory flows.

The device has been used for a wide variety of cases with spontaneous and intermittent positive pressure ventilation. Other breathing systems have been described,[6,7] but these involve levers, adjustment of valves, replacement of reservoir bags by ventilator supply tubing and switching the ventilator on or off. The system described here only requires switching of the ventilator.

It is essential that the APL valve is fully open in both modes of ventilation and, preferably, it should be modified accordingly. If the APL valve is closed, this would quickly become apparent from distension of the reservoir bag and a positive pressure, indicated by the ventilator pressure gauge which remains operative at all times.

Although the device is described for use with a Nuffield 200 ventilator, it may also be used with other ventilators capable of powering a Bain system.

Acknowledgments

The author is grateful to Mr B. Trussler, Senior Operating Department Assistant, for his help in constructing the device, to Mr. R. Reading, Operating Department Assistant, for his photographic assistance and to Mrs M. Kelly for her secretarial skills.

References

1. Spoerel WE, Aitken RR, Bain JA. Spontaneous respiration with the Bain breathing circuit. *Canadian Anaesthetists' Society Journal* 1978; **25:** 30–5.
2. Editorial Note. *Anaesthesia* 1981; **36:** 636.
3. Adams AP, Henville JD. A new generation of anaesthetic ventilators. *Anaesthesia* 1977; **32:** 34–40.
4. Adams AP. The Bain Circuit. *Anaesthesia* 1977; **32:** 46–9.
5. Nunn JF. *Applied respiratory physiology*. London: Butterworths, 1969: 83.
6. Humphrey D. A new anaesthetic breathing system combining Mapleson A, D and E principles. *Anaesthesia* 1983; **38:** 361–72.
7. Burchett KR, Bennett JA. A new co-axial breathing system. *Anaesthesia* 1985; **40:** 181–7.

Anaesthesia, 1986, Volume 41, pages 635–637

Forum

Intravenous fluids in minor surgery. Their effect on recovery from anaesthesia

P.W. Keane, MD, FFARCS, FFARCSI, Consultant, P.F. Murray, MB, BCh, BAO, Senior House Officer, Department of Anaesthesia, Regional Hospital, Newcastle Road, Galway, Ireland.

Summary

The value of infusing a total of 2 litres of intravenous fluids intra- and postoperatively was assessed in 212 fasting patients undergoing minor surgery procedures. The treated patients (108) recovered from the effects of surgery and anaesthesia more quickly than patients without fluids (104). The results of improved quality of the postoperative recovery, a shorter hospital stay and earlier return to work, especially in those patients who had some difficulty in recovering from anaesthesia on previous occasions, encourages the more frequent use of intravenous fluids in minor surgery.

Key words

Fluid balance; recovery.

The value of maintaining normovolaemia in minor and major surgical stress situations was highlighted by Shires and his colleagues in 1961.[1] Application or modification of their concepts fundamentally changed thinking regarding the volume of electrolyte solutions or 5% dextrose in water required during surgery, and their value in maintaining cardiovascular homeostasis.

The benefit of intra-operative intravenous fluids and especially the concept of preload has been investigated by assessing antidiuretic hormone (ADH) levels.[2] urinary volume and solute excretion,[3] aldosterone response and acute renal failure postoperatively. All of these investigations refer to fluid therapy during major surgery. A search of the literature does not reveal any study in relation to the value of intravenous fluids for minor operative procedures and their effects on the rate of recovery and the patient's well-being following surgery and anaesthesia.

Methods

For the purpose of this study, 212 patients between the ages of 18 and 50 years were chosen. Ethical consent was obtained from the clinical research ethical committee. The mean age of this group was 31 years and all patients were classed in ASA groups 1 or 2.

Patients were randomly allocated into one of two groups. The treated group received intravenous fluids through a peripheral venous cannula (JELCO), while the other did not. The fluids administered consisted of 1 litre Hartmann's solution peroperatively and 1 litre 5% dextrose in water postoperatively. The patients were unaware of the purpose of the intravenous fluid.

A standard anaesthetic induction technique of fentanyl 0.001 mg/kg and thiopentone 4 mg/kg was used. Anaesthesia was maintained using halothane 1–1.5% inspired concentration, during which all patients breathed spontaneously. None was intubated.

Two methods of assessment were used. The first was in the form of three questionnaires. Questionnaire number 1 was answered 6 hours postoperatively, when the patients were questioned as to the presence or absence of nausea, vomiting, thirst, dizziness, drowsiness and headache. Questionnaire number 2 was completed by the patient on the third postoperative day and sought to assess postoperative well-being compared to pre-operative status. Questionnaire number 3 was sent one month postoperatively to those patients who had had a previous anaesthetic. They were asked to compare this most recent anaesthetic to their previous experience (i.e. better, the same or worse).

The second method of assessment used was serial measurement of serum osmolalities using a micro-osmometer (Herman Roebling, Model 8301015), to add an objective measurement to our findings. Blood samples were taken from all patients at booking, at induction of anaesthesia and 6 hours postoperatively. The mean of two determinations was taken.

Results

Of 212 patients studied, 108 had intravenous fluids and 104 did not.

The surgical procedures included breast biopsies (60),

0003–2409/86/060635 + 14 $03.00/0 © 1986 The Association of Anaesthetists of Gt Britain and Ireland

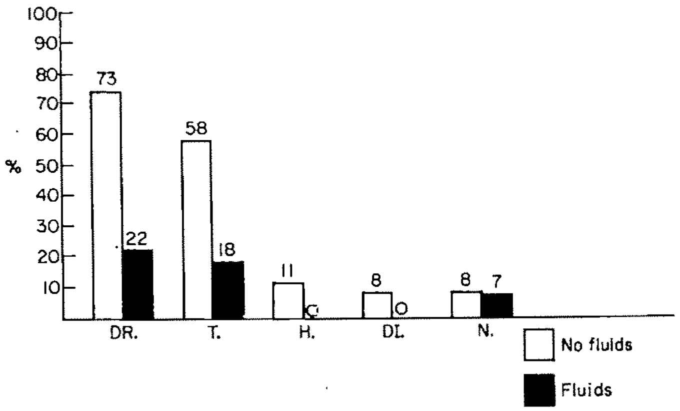


Fig. 1. The results of the first questionnaire. The presence of symptoms listed are expressed as a percentage of replies and compared between those who had fluids ($n = 108$) and those who did not ($n = 104$), (DR), drowsiness; (T), thirst; (H), headache; (DI), dizziness; (N), nausea.

varicose vein ligations (72), dilatation and curettage (64) and inguinal hernia repairs (16). The duration of the procedures was between 10 and 45 minutes. The mean duration was 18 minutes. The weight of the patients ranged between 55 and 81 kg with a mean value of 67 kg.

The results of the questionnaires were as follows: all number 1 questionnaires were completed at 6 hours postoperatively. As can be seen from Fig. 1, there was a clinically significant reduced incidence of these symptoms in those patients who had received intravenous fluids; 22% complained of drowsiness, whereas in the group who did not have fluids the equivalent incidence was 73%. Only 18% of these treated complained of thirst, as compared to 58% of the others. There were no complaints of headache or dizziness from those who had fluids, while the figures were 11% and 8% respectively in the group not having fluids.

There was an 83% (176) response to questionnaire number 2, of whom 84 had received fluids and 92 did not. As can be seen from Fig. 2, of those who had fluids, 95% replied that at 3 days postoperatively they felt no different than pre-operatively, whereas 5% said that they felt worse. In the group that did not have fluids, 49% said they felt worse and 51% said they felt the same.

The reply rate to questionnaire number 3 was 92 out of 120 (76%) who had had previous anaesthetics. As can be seen from Fig. 3, those who said the most recent anaesthetic had been better comprised 93% of the group that had intravenous fluids, but only 3% of the group that did not have fluids. Those who reported that the effects of the anaesthetic were the same, consisted of 4% of the group who had had fluids and 66% who had not. Thirty-one percent of those who did not have fluids said that the most recent anaesthetic was worse, while the figure was 3% in those who did have fluids. It was not recorded whether intravenous fluids had been given during the previous anaesthetic.

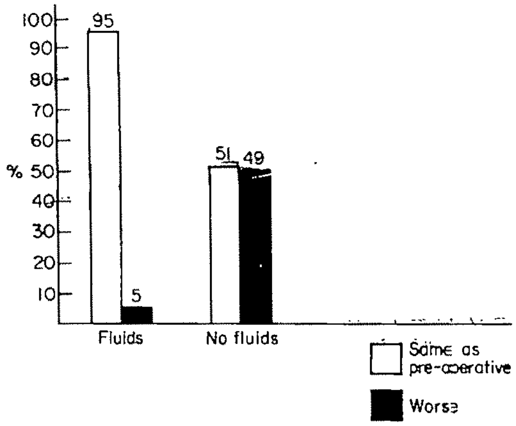


Fig. 2. The response to the second questionnaire. The subjective feeling of well-being is expressed as a percentage of total replies. Those who had fluids ($n = 82$) are compared to those who did not ($n = 92$). (□), same as pre-operative; (■), worse

The serum osmolalities were accepted as an objective method of substantiating this evidence and we found no statistically significant difference in the serum osmolalities between the two groups in the pre-operative samples. In group 1, given fluids, the mean value was 299 mosm/litre and in group 2, without fluids, the mean value was 298 mosm/litre. However, post-operatively the mean value in those who had fluids was 295 mosm/litre, whereas in those who did not have fluids it was 308 mosm/litre. This difference was found to be statistically significant with a p value <0.05. (Statistical method: Student *t*-test.)

This result is in agreement with the findings of the questionnaires, which suggest that those patients who received intravenous fluids were rehydrated post-operatively.

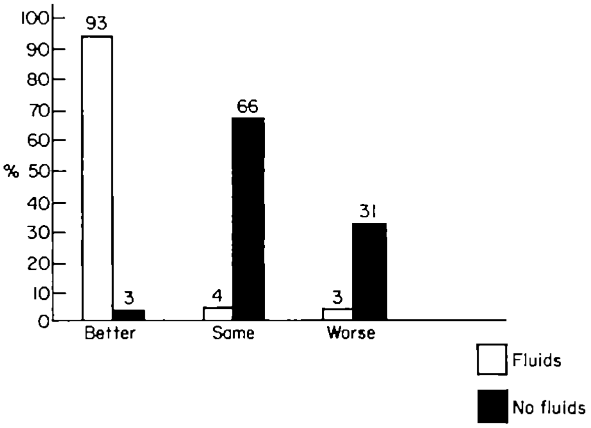


Fig. 3. The reply to the third questionnaire shows how patients themselves rated the most recent anaesthetic compared to previous anaesthetics for similar procedures. ($n = 92$). (□), fluids; (■), no fluids.

Discussion

Fasting from fluid and food from the night before implies that a degree of dehydration is inevitable from insensible losses. Thus, a 70 kg adult who presents for morning surgery is already likely to be at least 1 litre of fluid dehydrated. This depletion may not be of any real importance out of a total body fluid volume of 50 litres. However, the fluid balance homeostasis mechanism is controlled so that the metabolic response is finely activated even with this small loss.[4]

The results show that the relatively small volume of infused fluids can have significant effect on the patient's well-being immediately postoperatively, presumably due to correction of a minor degree of dehydration. The general effect on the patients is such that some days postoperatively, 93% of those who had intravenous fluids considered that the most recent anaesthetic was better than past experiences.

Acknowledgment

The authors wish to acknowledge the help of Dr Helen Grimes, Consultant Biochemist, Regional Hospital, Galway.

References

1. Shires T, Williams J, Brown F. Acute change in extracellular fluids associated with major surgical procedures. *Annals of Surgery* 1961; **154**: 803–10.
2. Moran WH, Zimmermann B. Mechanisms of antidiuretic hormone (ADH) control of importance to the surgical patient. *Surgery* 1967; **62**: 639–44.
3. Ichikawa Y, Kawagoc M, Nishikai M, Yoshida K, Homma M. Plasma corticotrophin (ACTH), growth hormone (GH) and 11-OHCS (hydroxycorticosteroid) response during surgery. *Journal of Laboratory and Clinical Medicine* 1971; **78**: 882–90.
4. Milligan RC. In: *Shock and hypotension.* Mills LC, Mayer JH (Eds), New York: Grune and Stratton, 1975.

Anaesthesia, 1986, Volume 41, pages 637–640

Hypotensive anaesthesia for microsurgery of the middle ear. A comparison between isoflurane and halothane

M.L. Fairbairn, BM, BCh, FFARCS, Registrar, R.J. Eltringham, MB, ChB, FFARCS. Consultant, P.N. Young, MB, FFARCS, Consultant, J.M. Robinson, MB, FRCS, Consultant, Departments of Anaesthesia and Otorhinolaryngology, Gloucestershire Royal Hospital, Great Western Road, Gloucestershire.

Summary

Fifty patients undergoing microsurgery of the ear were anaesthetised using thiopentone, nitrous oxide, oxygen and either *halothane or isoflurane, via a low flow circle system with carbon dioxide absorption. Systolic blood pressure was reduced to approximately 70 mmHg by the additional use of increments of labetalol; the patients breathed spontaneously. The degree of haemostasis was assessed by the surgeon who was unaware which volatile agent was being used to supplement anaesthesia. Isoflurane, although it is a potent vasodilator produced operating conditions which were indistinguishable from halothane. Isoflurane is thus a safe and reliable alternative to halothane as a volatile agent used to supplement anaesthesia when using induced hypotension for middle ear surgery.*

Key words

Anaesthetic techniques; hypotension, induced.
Anaesthetics, volatile; isoflurane, halothane.

Methods

Fifty patients (ASA Class 1) aged between 12 and 70 years, scheduled for microsurgery of the ear, were studied. Informed consent was obtained and the patients randomly allocated to receive halothane or isoflurane. A standard premedication of pethidine 1.5 mg/kg, promethazine 25 mg and diazepam 0.3 mg/kg was administered 1.5 hours before surgery. Anaesthesia was induced with thiopentone 4 mg/kg, followed by suxamethonium 1.5 mg/kg and 4% lignocaine spray to the larynx, prior to intubation of the trachea. Anaesthesia was then continued with oxygen, nitrous oxide and either halothane or isoflurane via a circle system, including soda lime, with the patients breathing spontaneously

Once a steady state had been achieved with flow rates of oxygen of 4 litres/minute and nitrous oxide of 4 litres/minute for 10 minutes, the flow rates were reduced and the circle system fully closed. Basal oxygen requirements were then delivered and the volatile agents administered by a Goldman vaporizer placed within the system. The concentration of halothane was in the range 1–1.5% and isoflurane in the range 1.5–2%, based on their known minimum alveolar concentration (MAC) values.[1,2]

Before surgery commenced, the skin behind the ear was infiltrated with 4 ml of 3% prilocaine, containing 1:300 000 adrenaline and the patients were positioned with a 15° head up tilt. Labetalol was used to achieve a satisfactory level of hypotension and was administered intravenously in 10 mg increments. The systolic pressure was lowered by this technique to 70 mmHg.

The ECG was continuously displayed and observed for any abnormalities and the blood pressure was measured directly following arterial cannulation. The inspired oxygen concentration was displayed by an oxygen analyser, and the concentration of the halogenated anaesthetic agent was measured (Engström Emma). The patients received the same intravenous fluid regime, consisting of one litre of Hartmann's solution during surgery, followed by one litre of 5% dextrose during the succeeding 8 hours.

All operations were performed by the same surgeon (JMR) who was unaware which volatile agent was being used. He assessed the operative field and graded the results using a standard numerical scoring system as previously described.[3] The surgeon also assessed the operating field on a linear analogue scale ranging from 0 (bloody) to 10 (very dry).

In 20 patients (10 in each group), arterial blood was taken one hour after induction for blood gas analysis.

Results

Twenty-five patients in this series received halothane and twenty-five received isoflurane. The age, weight and sex distributions between the two groups were comparable (Table 1). The surgeon described the operating field as adequate in all patients. Table 2 shows the distribution of the patients with the degree of haemostasis achieved and the mean values on the linear analogue scale for the two volatile agents. There was no statistically significant difference by the Chi squared test, applied to the haemostasis scores achieved by the halothane and isoflurane groups. The mean doses of labetalol used to achieve the desired reduction of blood pressure were very similar (Table 3).

The mean duration of surgery was 1 hour 24 minutes in the halothane group and 1 hour 29 minutes in the isoflurane group. The mean rate of volatile agent used during each anaesthetic was measured and found to be

Table 1. Mean (SD) age, mean weight and sex distribution in the halothane and isoflurane groups

	Halothane group	Isoflurane group
Mean age (years)	34 (14)	31 (15)
Mean weight (kg)	70 (14)	65 (14)
Sex distribution		
Male	11	13
Female	14	12

Table 2. The surgeon's assessment of the operating field

	Halothane group	Isoflurane group
Haemostasis score		
Excellent haemostasis	5	6*
Good haemostasis	13	14*
Adequate haemostasis	7	5*
Analogue scale		
Mean (SD) value on analogue scale 0–10	4.65 (0.79)	4.67 (0.81)

*Chi squared = 0.461.

Table 3. Mean doses and range of labetalol used to achieve the desired level of hypotension

	Halothane group (mg)	Isoflurane group (mg)
Mean dose of labetalol	52	60
Range	10–150	10–170

Table 4. Intra-operative blood gas analysis (mean value)

	Halothane ($n = 10$)	Isoflurane ($n = 10$)
$Pa\text{O}_2$ (kPa)	29	32
$Pa\text{CO}_2$ (kPa)	8.2	8.2
pH	7.22	7.22
Base excess	−2.6	−2.8

4.8 ml/hour of halothane and 6.5 ml/hour of isoflurane. Continuous display of the electrocardiogram (lead CM5) showed no change in rhythm or of the ST segment in any patient.

Blood gas analysis showed a mixed respiratory and metabolic acidosis in both groups (Table 4).

Discussion

The surgical field in microsurgery of the middle ear must have good haemostasis for surgery to be performed to an adequate standard, and deliberate hypotension is commonly performed. The technique of using a volatile anaesthetic agent with spontaneous ventilation and addition of an intravenous agent further to reduce the blood pressure is an acceptable method of inducing hypotension. As discussed in a previous study[3] (which compared halothane and enflurane in a similar technique) spontaneous ventilation has the advantages that the negative intrathoracic pressure during inspiration aids venous drainage and helps to maintain a dry operative field. Adequate cerebral perfusion in the presence of a low arterial pressure is also ensured by a reasonable cerebral arteriovenous pressure gradient and the slight hypercarbia produced. In the absence of electroencephalography or a cerebral function monitor the regularity of breathing has been considered by some to indicate the adequacy of cerebral perfusion during hypotension.

As isoflurane is an expensive agent, a closed circle system was used. The advantages of this system, i.e. both the conservation of anaesthetic gases and volatile agents and the reduction of atmospheric pollution, are well known. The current cost of isoflurane is much more than that of halothane,[4] but with this method its use is cost effective. The potency of isoflurane, as measured by MAC (1.15%) is less than halothane (0.75%). However, isoflurane has a much lower rubber gas partition coefficient and is stable in soda lime.[5] Consequently, there is less wastage with isoflurane. The rate of isoflurane used was greater than the rate of halothane used, but because of the very small volumes involved with this technique, there was little difference in the overall cost of surgery in the two groups.

This study has shown that satisfactory operating conditions can be achieved using either of these agents as part of the anaesthetic technique, and there was no statistical difference between the two groups. The advantages of isoflurane over halothane are well established, and several of the properties of isoflurane may make it a better choice for this type of anaesthesia. For example, its much lower level of biotransformation,[6] (0.17% of uptake is recovered as metabolites with isoflurane, compared to 20% for halothane), could be an advantage in middle ear surgery where repeat operations are common. Also, the low renal toxicity of isoflurane is advantageous in a technique where renal blood flow is reduced. Furthermore, isoflurane has been shown to be less depressant to the heart than halothane, by several indices,[7,8,9] and this is an advantage when hypotensive anaesthesia is induced. Finally, the fact that dysrhythmias are less likely to arise is of particular importance when adrenaline is injected as part of the surgical technique,[10] and the anaesthetic results in a respiratory acidosis.

Conclusion

It is concluded that with the techniques described, satisfactory operating conditions can be achieved for microsurgery of the middle ear using either halothane or isoflurane to supplement anaesthesia during hypotension induced by labetalol. Isoflurane provides a safe and reliable alternative to halothane, is inexpensive when used in the closed system and its physical and pharmacological properties could be of particular advantage in this branch of surgery.

References

1. Saidman LJ, Eger EI, Munson ES, Babad AA, Muallem M. Minimal alveolar concentration of methoxyflurane, halothane, ether and cyclopropane in man: correlation with theories of anesthesia. *Anesthesiology* 1967; **28:** 994–1002.
2. Stevens WC, Dolan WM, Gibbons ET, White A, Eger EI II, Miller RD, De Jong RH, Elashoff RM. Minimal alveolar concentrations (MAC) of isoflurane with and without nitrous oxide in patients of various ages. *Anesthesiology* 1975; **42:** 197–200.
3. Eltringham RJ, Young PN, Fairbairn ML, Robinson JM. Hypotensive anaesthesia for microsurgery of the middle ear. A comparison between enflurane and halothane. *Anaesthesia* 1982; **37:** 1028–32.
4. Prys-Roberts C. Isoflurane. *British Journal of Anaesthesia* 1981; **53:** 1243–5.
5. Eger EI. Isoflurane; A review. *Anesthesiology* 1981; **55:** 559–76.
6. Mazze RI, Cousins MJ, Barr GA. Renal effects and metabolism of isoflurane in man. *Anesthesiology* 1974; **40:** 536–42.
7. Stevens WC, Cromwell TH, Halsey MJ, Eger EI, Shakespeare IF, Bahlman SH. The cardiovascular effects of a new inhalational anesthetic, Forane, in human volunteers at constant arterial carbon dioxide tension. *Anesthesiology* 1971; **35:** 8–16.

8. MERIN RG, BASCH S. Are the myocardial functional and metabolic effects of isoflurane really different from those of halothane and enflurane? *Anesthesiology* 1981; **55**: 398–408.
9. LYNCH C III. Differentiated effects of volatile anesthetics upon myocardial excitation-contraction coupling. *Anesthesiology* 1984; **61**: A85.
10. JOHNSTON RR, EGER EI, WILSON C. A comparative interaction of epinephrine with enflurane, isoflurane and halothane in man. *Anesthesia and Analgesia* 1976; **55**: 709–12.

Anaesthesia, 1986, Volume 41, pages 640–643

Intravenous anaesthesia with propofol and alfentanil. The influence of age and weight

P. Hilton, MB, BS, FFARCS, Senior Registrar, V.J. Dev, MB, BS, Registar and E. Major, MB, BS, FFARCS, Consultant, Department of Anaesthetics, Morriston Hospital, Swansea SA6 6NL.

Summary

Sixty healthy patients undergoing body surface surgery were anaesthetised with continuous infusions of propofol (200 µg/kg/minute) and alfentanil (0.25 µg/kg/minute). Additional bolus doses of propofol (20 mg) were given if movement occurred. The incidence of patient movement in response to skin incision was significantly less in patients over 45 years of age than in those below 45 years ($p < 0.05$). Maintenance dosage of propofol sufficient to abolish movement decreased with increasing age ($p < 0.001$). Systolic blood pressure decreased in most patients over the first 10 minutes of anaesthesia and the magnitude of this decrease increased with age ($p < 0.0001$). These parameters did not correlate strongly with body weight. Dose requirements of propofol are not the same for patients of all ages and strongly suggest that young and old patients should not be treated as a homogeneous group, either for investigative or clinical purposes

Key words

Anaesthetics intravenous; propofol, alfentanil.

The theoretical attractions of total intravenous anaesthesia (TIVA) have led to the extensive investigation of constant infusion techniques as a method of delivering anaesthetic agents.[1] Morgan[2] has pointed out that the aim of TIVA 'is to achieve a concentration of drug in the blood stream which will result in the required depth of anaesthesia'. It follows, therefore, that there is a need to define the dose of drug required to achieve the desired effect. The concept of minimum infusion rate (MIR) goes some way towards meeting this requirement. Prys-Roberts introduced MIR as a minimum alveolar concentration (MAC) equivalent for intravenous agents[3] and defines it as that rate of infusion of an intravenous anaesthetic which would prevent movement in response to skin incision in 50% of patients.

It is well known amongst clinical anaesthetists that certain types of patient, notably the elderly, require less anaesthetic dosage than others and this has been confirmed for thiopentone by Christensen and colleagues.[4] However, they demonstrated that the plasma venous concentration at the onset of sleep was similar in old and young men, suggesting that the elderly require less drug to achieve a comparable blood level. It is also now understood that the elderly do not eliminate or redistribute drugs as fast as their younger counterparts. It seems likely, therefore, that the dosage of intravenous anaesthetic required to maintain a given blood level might be less in the elderly and, conversely, that a standard dose might be more effective in preventing patient movement as age increases.

It has become traditional for intravenous agents to be administered in dosage according to body weight, but it may not be sound practice to increase dosage to compensate for increased body weight. We have therefore carried out an investigation to assess the effect of age and weight on the ability of a continuous infusion of propofol and alfentanil to prevent movement in response to skin incision.

Method

Sixty healthy patients undergoing body surface surgery gave written informed consent to receive an infusion of

---

Correspondence should be addressed to Dr E. Major please.

propofol and alfentanil. Local ethics committee approval was obtained. Patients were admitted into the study such that half were below 45 years and half over 45 years. It was also arranged that equal numbers of patients in each age group were above and below 70 kg.

All patients were premedicated with temazepam (20 mg) approximately 90 minutes prior to surgery. The anaesthetic technique was standardised and all patients received identical anaesthetic dosage, adjusted for body weight. Prior to induction, alfentanil (5 μg/kg) was administered into a forearm vein and immediately followed by an infusion of alfentanil (0.25 μg/kg/minute). One minute later, anaesthesia was induced with propofol (2.5 mg/kg) administered over 20 seconds into the same cannula. This was followed by gallamine (20 mg) to reduce suxamethonium pains, and a constant infusion of propofol (200 μg/kg/minute). Tracheal intubation followed suxamethonium (1 mg/kg), inflation with oxygen and lignocaine spray to the larynx. Manual ventilation was continued till the onset of spontaneous respiration. Patients were allowed to breathe 100% oxygen throughout the procedure. Twelve minutes after induction, the surgeon was asked to make the initial skin incision and the patient's response to this was recorded.

In the event of the patient coughing or moving in response to stimulation, a bolus of propofol (20 mg) was administered. The incidence of such events was noted. The infusion rates of propofol and alfentanil were kept constant throughout surgery and were discontinued with the last skin suture. Recovery times were recorded, as were any untoward events occurring during or after the anaesthetic.

Monitoring. Baseline readings of systolic pressure, diastolic pressure and heart rate were taken prior to induction and repeated every minute thereafter, using an automated blood pressure recorder (Dinamap 845, Critikon). Respiratory rate was monitored every 5 minutes for the first 30 minutes.

The data were analysed statistically using the Chi squared test, Student's paired *t*-test and regression analysis.

Results

The sixty patients were aged from 19–69 years (mean 44.4 years) and their weights ranged from 45–89 kg (mean 68.2 kg).

The intravenous anaesthetic technique proved adequate to maintain surgical anaesthesia in all patients, but 40 of the 60 patients needed supplements of propofol to maintain anaesthesia. Thirteen patients needed four or more bolus doses (20 mg) of propofol and one exceptional patient received 13 bolus doses in all. The duration of anaesthesia varied enormously, from 17 minutes to 198 minutes, and consequently, total dose of propofol also varied.

The majority (65%) of patients were able to open their eyes to command within 15 minutes of the end of the anaesthetic infusion, but in three patients recovery was prolonged beyond 25 minutes. There was a strong positive correlation ($r = 0.49$) between total propofol dosage and recovery time ($p < 0.001$).

There was a highly significant ($p = 0.001$) negative correlation ($r = -0.37$) between increasing age and the overall mean rate of propofol utilisation defined as the maintenance dosage of propofol (including boluses) divided by duration of unconsciousness and expressed as μg/kg/minute (Fig. 1).

The mean time to initial skin incision was 12.3 min-

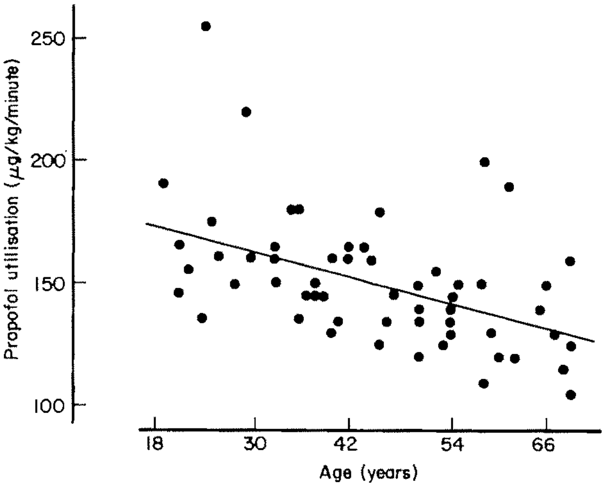


Fig. 1. Propofol utilisation (infusion dose and bolus dose expressed per kilogram divided by the duration of unconsciousness) plotted against age for each patient ($p < 0.001$). Three observations are obscured. $r = -0.37$.

Table 1. Incidence of movement during the first 5 minutes of surgery for patients within one standard deviation (14.4 years) of the overall mean age (44.4 years) and for those more than one standard deviation above or below the mean

	< 30 years	< 44.4 years	> 44.4 years	> 58.8 years
Movement in response to surgery (number of patients)	8	7	6	1
No movement (number of patients)	2	13	13	10

utes (SD 1.11 minutes). The incidence of patient movement during the 5-minute period following skin incision significantly decreased with age (Table 1). Of those patients aged below 30 years, 80% moved in the 4 minutes following skin incision. Movement occurred in only 9% of patients over 58.8 years, and this difference was statistically significant ($p < 0.01$). The incidence of movement also decreased with increasing body weight, but was not statistically significant. Below 56.6 kg (mean − 1 SD) the incidence of movement was 40% (4/10) whilst above 79.8 kg (mean + 1 SD) the incidence was only 14% (2/14). This difference was not significant.

Mean systolic and diastolic blood pressures had decreased significantly ($p < 0.001$) by 10 minutes after induction of anaesthesia (Fig. 2). Following the start of surgery, however, both pressures increased. There was a highly significant ($p = 0.0001$) positive correlation between age and the magnitude of systolic pressure decrease at 10 minutes ($r = 0.47$). There was no such relationship between systolic pressure and body weight. Mean heart rate increased over the first few minutes of anaesthesia, but subsequently returned to pre-induction levels (Fig. 2).

The mean time of onset of spontaneous respiration varied considerably between patients. Thirty-two patients were still apnoeic prior to skin incision; 27 of these resumed spontaneous ventilation shortly after skin incision. Five patients remained apnoeic throughout surgery. There was no correlation between duration of apnoea and age or body weight.

Prediction of patient movement. Overall, 22 patients out of 60 moved at least once in the 5-minute period following skin incision. The majority of these (68%) were less than 45 years of age.

Thirty-two patients were still apnoeic 10 minutes after induction, but eight of these moved at skin incision shortly afterwards. Of those patients with a respiratory rate of 16/minute or more at 10 minutes, the majority (13/22) moved at skin incision. By contrast, amongst those patients breathing at less than 16 breaths/minute, the incidence was only 25% (9/38). This was a statistically significant difference ($p < 0.01$).

There were no significant differences in the magnitude of heart rate or systolic pressure changes when those patients who moved at skin incision were compared to those who did not. However, the incidence of movement was high (50%) in patients whose heart rate increased by more than 20 beats/minute over the first 10 minutes of anaesthesia. A similar high incidence was found in those patients whose respiratory rate exceeded 16/minute and in those patients where systolic pressure had decreased by less than 20 mmHg at 10 minutes.

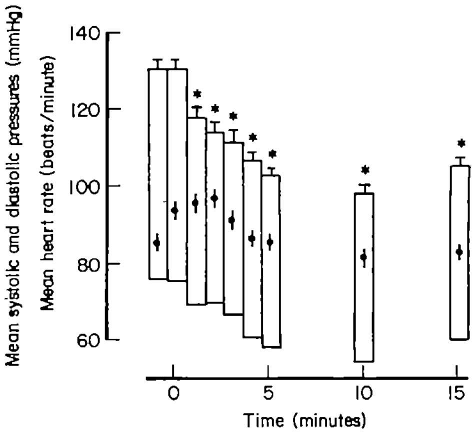


Fig. 2. Mean systolic (SEM) and diastolic pressures (vertical bars) and mean heart rate (●, SEM) for all patients plotted against time from just before induction (T-1) until just after skin incision (T + 15). *denotes $p < 0.001$.

Discussion

This study was designed to investigate the effect of age and weight on the response of patients to surgical stimuli during intravenous anaesthesia with propofol and alfentanil. Alfentanil was used to supplement propofol since our previous experience has suggested that analgesic supplements aid smooth anaesthesia. The dose used was very low but, nevertheless, it must have contributed to the respiratory depression seen in many of our patients. There was no attempt to alter infusion rates in the light of events, although a bolus of propofol (20 mg) was administered in the event of patient movement. As a result, some patients may have received much larger doses than necessary and the dosages quoted here should not necessarily be taken as optimum. This is reflected by the fact that five patients remained apnoeic almost throughout surgery and systolic pressure had fallen by more than 50 mmHg in twelve patients immediately prior to surgery. Surgical stimulation increased blood pressure in the majority of cases. The answer to the problem of hypotension is, unfortunately, not the simple one of reducing dosage, because patients occasionally moved even when blood pressure was low. It has been shown that propofol in the Cremophor EL preparation principally affects systemic vascular resistance,[5,6] so that an infusion of fluid ought to correct hypotension. We did not have to resort to this for any of our patients.

Older patients receiving propofol and alfentanil were much less likely to move in response to surgery than their younger counterparts. The incidence of movement was 80% below 30 years and 9% above 59 years. There was a significant negative correlation between age and the dosage required to maintain anaesthesia. There was also a significant positive correlation between age and the magnitude of blood pressure decrease, in spite of the fact that the older patients received less drug. There was no significant association between body weight and any of these parameters.

These findings are difficult to explain in the absence of detailed pharmacokinetic data for propofol in the normal, obese and elderly patient, but Homer and Stanski[7] have demonstrated a smaller than usual central compartment volume for thiopentone in the elderly. If this should also prove the case for propofol, then the resulting higher blood level following an induction dose might partly explain our findings. Redistribution of injected drugs may also be slower in the older patient, with the effect of maintaining a high blood level for longer.

The blood level of both propofol and alfentanil would undoubtedly still be rising at the time of skin incision in all the patients studied, since we did not allow sufficient time to achieve steady state. By adopting a time of 12 minutes for initial skin incision, we have attempted to mimic normal clinical practice at the same time as standardising the conditions for all patients.

The mean recovery time of 15 minutes is acceptable when it is realised that no attempt had been made to reduce the infusion rate until surgery had been completed. The strong positive correlation between total anaesthetic dosage and recovery time does not necessarily suggest that cumulation had occurred, since many patients were not anaesthetised long enough to achieve a steady state blood level.

In conclusion, the fixed infusion rate (200 μg/kg/minute) of propofol used in this investigation was not sufficient for all patients, despite infusion of alfentanil (0.25 μg/kg/minute) but anaesthesia was maintained in all cases by the addition of propofol supplements. Increasing age appears to decrease the need for such supplements, but is associated with greater cardiovascular depression as measured by systolic pressure.

There is a need for further investigation of the effects of age and body weight on anaesthetic dosage, but clearly it is not correct to assume that dose requirements of intravenous agents are the same for patients of all ages.

Acknowledgments

We are grateful to the many nursing, surgical and anaesthetic colleagues who helped us with the investigation. Our thanks are also due to Imperial Chemical Industries for their support of the study and to Miss Shân Jones who typed the manuscript.

References

1. Dundee JW. Total intravenous anaesthesia. *British Journal of Anaesthesia* 1978; **50**: 89–90.
2. Morgan M. Total intravenous anaesthesia. *Anaesthesia* 1983; **38**: suppl. p. 1–9.
3. Prys-Roberts C. Cardiovascular effects of continuous intravenous anaesthesia compared with those of inhalational anaesthesia. *Acta Anaesthesiologica Scandinavica* 1982; **26**: suppl. 75, 10–7.
4. Christensen JH, Andreasen F, Jansen JA. Pharmacokinetics of thiopentone. A comparison between young and elderly patients. *Anaesthesia* 1982; **37**: 398–404.
5. Aun C, Major E. The cardiorespiratory effects of ICI 35 868 in patients with valvular heart disease. *Anaesthesia* 1984; **39**: 1096–100.
6. Al-Khudhairi D, Gordon G, Morgan M, Whitwam JG. Acute cardiovascular changes following disoprofol. Effects in heavily sedated patients with coronary artery disease. *Anaesthesia* 1982; **37**: 1007–10.
7. Homer TD, Stanski DR. The effect of increasing age on thiopental dose requirement. *Anesthesiology* 1983; **59**: A530.

Anaesthesia, 1986, Volume 41, pages 643–648

Treatment of near drowning—a review of 130 cases

A.D. Simcock, FFARCS, Consultant Anaesthetist, Royal Cornwall Hospital (Treliske), Truro, Cornwall.

Summary

This paper reviews the management and clinical course of patients after rescue from near drowning. Those with adequate ventilation on arrival at hospital had an excellent prognosis. The prognosis of those patients with inadequate ventilation, or who have suffered cardiac arrest, depends on rapid assessment and the institution of vigorous resuscitative measures. The medical management of all types of patients is reviewed in detail, the results tabulated and complications discussed.

Key words

Drowning.

Immersion incidents in Cornwall are commonplace and In a 6-month period in 1984, the coastguard service co-ordinated the rescue of 225 casualties along 250 miles of coastline. There were 123 patients treated for near drowning during the period January 1974 to December 1984 inclusive. Only patients who had to be rescued from the water have been included, and not those who managed to reach the shore by their own efforts. In addition, a further nine were brought to hospital, but found to be dead and beyond resuscitation. There were 93 immersions in sea water, 27 in fresh water and three in tidal waters. The sea temperature around the shores varies from a minimum of 5.5°C in February to 15°C in September.

Assessment and management

The age range of the patients treated was from 18 months to 81 years, and the majority of patients were brought to hospital by helicopter. On landing the helicopter is met by a medical and nursing team, supported by portable equipment. The equipment consists of a basic resuscitation kit, comprising electrocardiogram, defibrillator and battery operated low reading thermometer. We have not found it practical to resuscitate the patient in the noisy vibrating atmosphere of the interior of the helicopter, but an assessment is made as soon as the patient lands and resuscitation commenced as the victim is removed from the helicopter. Initially, we assess whether the patient is breathing adequately and, indeed, whether he is breathing at all. Treatment is started before the patient is transferred to hospital. The initial stages of resuscitation depend on the findings of the assessment outlined above.

For purposes of further description, it has been our practice for some years to divide patients into four groups:[1] group 1, patients with no apparent inhalation, group 2, patients with inhalation, but apparently adequate ventilation, group 3, patients with inhalation, but inadequate ventilation, and group 4, patients with absent ventilation and cardiac output. The treatment of each of these groups will now be discussed in turn.

Group 1

These patients have been in sufficient difficulty to have been unable to save themselves and have had to be rescued from the water. They are admitted to hospital for at least 24 hours and observed for late onset of pulmonary or cerebral oedema. Normally, they are fully conscious and alert and it is now our policy to admit them to the wards rather than the intensive care unit. As well as a careful clinical examination, the following estimations are made:

Blood gas analysis. Despite the apparently normal clinical state, blood gas analysis frequently shows a metabolic acidosis. We have occasionally seen severe metabolic acidosis in patients who do not appear to have inhaled water. It would seem that there is some correlation between the degree of acidosis and the degree of hypothermia. If the arterial pH is less than 7.2, intravenous 8.4 percent sodium bicarbonate is given in a dose of 50 percent of the number of mmols calculated to bring the pH back to normal.

Temperature measurement. These patients are usually only mildly hypothermic and fully conscious, and only need treatment if the rectal temperature is below 35°C. Simple methods such as the use of a heated water blanket, warm woollen blankets and a space blanket usually suffice.

Laboratory investigations. These are limited to haemoglobin, packed cell volume, blood sugar blood urea and electrolytes. These investigations should be normal, as water has not entered the lungs. There has been no serious abnormality in any of these investigations in these patients.

Chest X ray. There have been no patients in this group where our clinical examination has not been borne out by a normal chest X ray. It seems that the presence of even small amounts of water in the lung is readily detected on auscultation.

Group 2

This is the commonest group of people seen and they are treated as follows.

Admission to the intensive care unit. Wherever possible, these patients are admitted to the intensive care unit for close monitoring. They frequently have respiratory distress and are cyanosed, with painful, wheezing respiration. Oxygen is administered by mask during their transfer. After recovery, they are kept in hospital for 48 hours after their chests are clinically and radiologically clear.

Oxygenation. It is of paramount importance that the progress of ventilation is watched both clinically and by blood gas analysis, in order to maintain a Pa_{O_2} of 8 kPa with an inspired oxygen percentage of not greater than 50 percent. This is normally done quite adequately by mask, but small children have occasionally been nursed in an oxygen tent.

Assessment and correction of hypothermia. Most patients are conscious or semiconscious, with temperatures ranging from 32–35°C. The simple methods already outlined, combined with the administration of warmed intravenous fluids are quite sufficient, as long as the patient's clinical condition remains stable.

Metabolic acidosis. There should be early blood gas analysis to assess the patient's acid base state and to maintain the pH above 7.2 with intravenous sodium bicarbonate.

Intravenous fluids. An intravenous infusion is set up on all these patients as soon as they arrive in the unit. In the case of salt water drowning, 5 percent dextrose is used and, conversely, normal saline in fresh water drowning. If peripheral perfusion is poor, then the question of the administration of plasma volume expanders should be considered. At present it would seem that Human Plasma Protein Fraction (HPPF) is the plasma volume expander of choice. All intravenous fluids should be passed through a blood warmer before administration.

Steroids. Intravenous steroids have been given to any patient who shows clinical or radiological evidence of inhalation, since the lungs may be at risk from damage from inhalation. Intravenous methylprednisolone 30 mg/kg is given as soon as the patient is admitted and repeated 8 hours later.

Intravenous antibiotics. It is difficult to accept that the aspiration of water into the lungs is a sterile process or that secondary infection will not occur in those who have inhaled water from swimming pools, the sea or rivers. Intravenous ampicillin or oral septrin are administered to patients with any evidence of inhalation.

Physiotherapy. This group of patients often complain of severe retrosternal pain and have wheezing respiration. However, as soon as the patient has recovered sufficiently to cooperate with the physiotherapist, as much inhaled water as possible should be removed by deep breathing and coughing.

Clinical investigations. Haemoglobin, packed cell volume, urea, electrolytes and blood sugar are measured as indicated, until the patient has recovered. There have been minor abnormalities in serum electrolytes in this group, mainly a small rise in sodium and chloride in salt water drowning, but these have resolved spontaneously, usually within 6–8 hours.

Radiology. Chest X ray usually confirms the clinical opinion and it is surprising how quickly the chest X ray reverts to normal after apparently fairly extensive initial pulmonary shadowing.

Group 3

Resuscitation. These patients should be assessed on arrival and intubated and ventilated as soon as possible. Patients are only transferred to the intensive care unit after tracheal intubation and suction and are ventilated with 100 percent oxygen during transfer.

Ventilation. Initial ventilation by means of a manual inflating bag is often accompanied by the necessity for frequent suction of water from the lungs. The maximum amount of water removed has been 2 litres. However, as soon as the need for frequent suction is overcome, the patients lungs are ventilated mechanically. A volume cycled machine is used because compliance is frequently reduced in the initial stages.

Positive end expiratory pressure (PEEP). If it is difficult to maintain a Pa_{O_2} of 8 kPa without the inspired oxygen concentration being greater than 50 percent, then we consider the use of PEEP. The latter can only be used when the cardiovascular state is satisfactory and commences with 0.25 kPa and the effect on pulse, arterial blood pressure and urine output are noted. If the initial PEEP regimen is tolerated, then it may be increased by 0.25 kPa increments up to 1.0 kPa.

Central venous pressure (CVP). Most patients have poor peripheral perfusion and a central venous pressure line should be set up as soon as is practical. There have not been any patients with raised central venous pressures during resuscitation from an immersion incident and any abnormality has always suggested hypovolaemia. We have used warmed intravenous fluids and a mixture of crystalloid and colloid solutions. In the past, blood was used as a volume expander and was satisfactory.

Hypothermia. Rectal temperatures have been as low as 26°C and several patients had temperatures in the range 28–30°C. If the patient's ventilation and cardiovascular system are stable, there is no need for rapid rewarming, but, if necessary, one of the safest and most effective methods of rewarming has been by peritoneal dialysis. Warmed isotonic peritoneal dialysis fluid is used. We have used this method on adults and in children down to the age of 5 years, and have found that insertion of the catheter is simple and safe and has produced no complications.

Basic regimens. After initial resuscitation, measurements should be made of blood sugar, acid base status, haemoglobin, packed cell volume and serum electrolytes. Treatment includes the use of intravenous steroids, antibiotics and physiotherapy. An occasional finding is a rapidly rising serum sodium and chloride level, accompanied by a rise in haemoglobin and packed cell volume in patients rescued from salt water. The majority of these return to normal without treatment. However, in the more serious cases, isotonic peritoneal dialysis will help minimise and correct electrolyte imbalance. To date, this has been rapidly successful and no patient has been dialysed for more than 24 hours.

Radiology. The chest X ray in these patients is usually virtually a 'white out' due to water in the alveoli, rather than left heart failure. With successful treatment, there is rapid improvement in the clinical and radiological picture, which frequently returns to normal in 48 hours.

Group 4

The most difficult to assess and treat are those patients who have apparently suffered a cardiac arrest, with absent ventilation and heart beat. Any patient with a short history of immersion is met by the resuscitation team, and is only declared dead after the following criteria have been considered: an adequate history has been obtained wherever possible, an ECG has been taken to show asytole, and a rectal temperature recording has been taken.

Using these criteria, of the 132 patients brought to us in over 10 years, only nine have not received an attempt at resuscitation. If the history is of a short immersion, particularly if hypothermia is present, then treatment would be initiated even if the heart was in asystole. Resuscitation techniques follow the conventional methods.

Intubation and ventilation. This is achieved as soon as the patient is assessed and transfer occurs during ventilation with 100 percent oxygen.

Cardiac massage. If the ECG shows asystole, then cardiac massage is undertaken and the patient transferred to the intensive care unit while undergoing cardiac massage and mechanical ventilation. Ventricular fibrillation is treated immediately by DC shock. Children have been successfully defibrillated at temperatures as low as 26°C.

Intensive care management. The parent's lungs are initially aspirated, and, when practical, are ventilated with a volume cycled ventilator and a CVP line set up. Warmed intravenous fluids are used as necessary, to establish a reasonable circulating blood volume and urine output. Metabolic acidosis, hypothermia and electrolyte imbalance may be severe in these cases and must be corrected. The most difficult to correct is hypothermia as the circulation is, of course, initially at a standstill. Any improvement in cardiac output with cardiac massage initially leads to the return of cold blood to the heart. Peritoneal dialysis and warmed nasogastric fluid has been tried in these patients, but with limited success. The inspired gas mixture of the ventilator is heated and humidified. The object should be to raise the temperature of the patient to 30–31°C. If resuscitation is successful, then future management will follow the lines previously outlined. If sinus rhythm and a reasonable cardiac output have been restored, then rewarming can be a gradual process. Even if resuscitation does not appear to be successful, it is not abandoned until the temperature has been raised to 31°C.

Results

It has been possible to review the treatment of 121 of the 123 patients treated. There have been 12 deaths and the remainder have survived and recovered normally. The survivors have been classified in the various groups used for assessment (Table 1).

Table 1. Number of survivors in the classification groups

	Number of patients	Survivors
Group 1	53	53
Group 2	50	49
Group 3	8	6
Group 4	10	1

All patients who had no clinical or radiological evidence of inhalation when they arrived at the hospital survived, none deteriorated and there were no serious sequelae. Many of these patients were said to have been apnoeic on rescue and had received mouth to mouth resuscitation.

The patients in group 2 also had a very good prognosis. The only death occurred in a patient who was not seen by the resuscitation team because he was thought to be suffering more from drunkeness than the effects of drowning. Four hours after admission he became hypotensive, cyanosed and unconscious. Although transferred to the intensive care unit and treated vigorously, he never recovered consciousness and subsequently died several weeks later from pulmonary embolism.

The six survivors in group 3 all recovered fully and suffered no pulmonary or cerebral damage. There were two deaths. The first was a child who was recovered from a submerged light aircraft. Initial resuscitation appeared to be successful but the patient subsequently died from respiratory distress syndrome (RDS). This is the only case of RDS that we have in our series, and the only serious pulmonary complication that occurred. The other death was in a patient who was unconscious on arrival and never recovered consciousness, but died several months later from pulmonary infection. Closer review of his history has suggested that the airway was not cleared before initial resuscitation was commenced on the beach.

In the patients who arrived having already apparently suffered cardiac arrest, there was only one survivor and he recovered normally. The heart was restarted in two further patients, but neither regained consciousness and death occurred after a short while from overwhelming cardiorespiratory failure. It should be noted that there were no mentally damaged survivors in our series and no long term pulmonary complications.

Discussion

Drowning occurs because of either an inability to swim or a decreased level of consciousness which leaves the airway unguarded. Frequently, there is a combination of both factors. There are, however, several medical conditions which can precipitate the drowning process and should always be borne in mind once the primary treatment has been instigated; examples are injuries to the head and neck causing temporary loss of consciousness, myocardial infarction, stroke, epilepsy, acute hypoglycaemia and intoxication with alcohol. Hyperventilation prior to diving can lead to sudden unconsciousness under the water because the $P\mathrm{ao}_2$ may fall to low levels whilst the $P\mathrm{aco}_2$ may still be low or normal. Sudden immersion in cold water can lead to hyperventilation and tetany.

It was first reported in 1969 that even accomplished swimmers may be unable to swim for more than a few minutes in very cold water.[2] There is little doubt that such people can drown through an inability to maintain normal swimming movements and keep their airway above the water well before they suffer from the other effects of hypothermia. The author has had discussions with life savers who recount similar experiences, in which expert warm water swimmers appeared to get into difficulty off the North Cornish coast; they produced bizarre paddling movements and had difficulty in coordination and control of their breathing and airway. On recovery, they steadfastly deny that they were in any difficulty whatsoever. The physiology of the drowning process has recently been reviewed by Golden,[3] who indicates that profound cardiovascular and respiratory changes occur during immersion and on removal from the water. It is also our experience that cardiac arrest occurring without apparent inhalation, the so-called dry drowning described by Moritz,[4] is a rare entity. This is difficult to explain satisfactorily, but a common finding of severe bradycardia in near drowned children may lend support to the concept of a vestigial diving reflex acting as a protective mechanism.[5]

It is apparent that a number of our patients did not have evidence of inhalation when first seen. Many patients who were apparently apnoeic when taken from the water and received mouth to mouth resuscitation had no evidence of inhalation on reaching hospital. These people need little treatment but careful observation, as late deterioration or secondary drowning has been well documented.[6,7] However, any patient who has inhaled water, should be admitted to an intensive care unit and carefully monitored. Even patients who are conscious and appear to be recovering quickly need watching for the cardinal signs of deterioration; these include a fall in the level of consciousness or a combination of tachycardia and tachypnoea. The detection and relief of hypoxia in the shortest possible time is fundamental to management. If there is any doubt about the adequacy of ventilation, then intubation and mechanical ventilation should be instituted without delay.

Cardiovascular stabilisation must accompany the relief of hypoxia. Any abnormality in the cardiovascular system has always been hypovolaemia. There have now been three clear instances where patients lost consciousness when lifted from the water in a vertical position. Inotropic agents have not been necessary as fluid replacement alone has proved satisfactory. Circulatory overload was not produced in any of our cases and there is no need for diuretics in initial therapy. Although facilities are available, we have not yet measured pulmonary artery or wedge pressures.

After these basic variables have been stabilised, the next priority is the acid base status of the patient and the question of hypothermia. These two problems seem closely linked, even if the circulation remains in a reasonably normal condition. We have abandoned any temperature correction of blood gas results as corrections were minor and did not affect clinical treatment. Hypothermia is common and we found that the records of 47 children admitted in a 6-year period showed that 45 percent of them had a rectal temperature of less than 35°C on arrival. At and above this temperature, cerebral function is usually normal and the airway is protected. If the temperature falls below 35°C, there is increasing mental impairment, disorientation and steady deterioration of consciousness. Eventually, the finest swimmer is unable to make the requisite effort to keep his airway above the water and he drowns. Our fatalities, though cold, all died from drowning and we saw no death primarily from hypothermia (which could only occur in a patient wearing a life jacket and immersed in a relatively calm sea).

Hypothermia must, however, be one of the major reasons why there have been reports of successful resuscitation after prolonged periods of immersion.[8–10] These have almost always occurred in children in whom the relatively large body surface area to weight ratio would mean that rapid cooling occurred in cold water. Cooling could also increase if cold water were absorbed from the gut or lung. We have successfully resuscitated one boy after 70 minutes of immersion in the water, despite cardiac arrest shortly before his arrival.

The methods used to increase body temperature have really been dictated by the facilities available to us, as we do not have the advantages of cardiopulmonary bypass, which has been used for controlled rewarming in accidental hypothermia.[11] Nevertheless, rapid rewarming probably has little place in treatment, because if the cardiac output and respiration are stable, there is little urgency in bringing the body temperature back to normal. There may be benefit from keeping the temperature at 31–32°C to aid recovery in those patients who have suffered from a cardiac arrest or hypoxia. Potential dangers from rewarming are sudden vasodilatation and a fall in blood pressure, coupled with the return of cold, acidotic blood to the heart.

The use of steroids has been controversial since the work of Calderwood,[12] which showed no improvement in survival rates after methylprednisolone. This was, however, restricted to aspiration of distilled water in dogs. We have continued, therefore, in the early use of large dose steroid therapy and have only one case of respiratory distress syndrome in our series.

Similarly, the routine use of antibiotics is controversial.[13] We have used a broad spectrum antibiotic in all patients who have aspirated and have had no problems with pulmonary infection, fibrosis, abscess or bronchiectasis.

The difference between fresh water and salt water drowning has largely become academic in initial treatment of immersion incidents. Transient changes in electrolyte balance after salt water drowning have been observed, but only rarely a serious clinical situation. It appears that isotonic peritoneal dialysis to reverse the situation and maintain normal electrolyte and water balance is a safe solution. Renal failure has been reported.[14]

Barbiturate therapy in comatose children suffering from fresh water near drowning was first advocated in 1979.[15] The use of barbiturates in conjunction with hyperventilation, dehydration and hypothermia aims to reduce the brain's metabolic needs and so minimise damage. Initial results were encouraging and, recently, Conn and Barker[16] showed that a specialised referral centre could produce remarkable recoveries, but a percentage of survivors had persistent cerebral damage. We rarely see this type of situation, because most patients arrive shortly after rescue, usually from salt water and, consequently, we have little experience of this form of treatment.

Future developments in treatment of the drowned patient lie largely at the accident site. Awareness of the dangers of cold water swimming are steadily being publicised,[17] but appropriate methods of rescue, resuscitation, and transport to hospital remain vital.

Acknowledgments

I would like to thank Mrs Anne Pearson for her endless patience and my three colleagues in the intensive care unit for their help over the years.

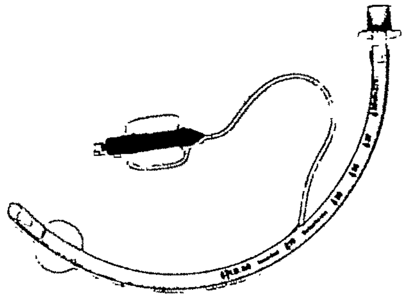
References

1. Simcock AD. Sequelae of near drowning. *Practitioner* 1979; **222:** 527–30.
2. Keatinge WR, Prys-Roberts, Cooper KE, Honour AJ, Haig J. Sudden failure of swimming in cold water. *British Medical Journal* 1969; **1:** 480–3.
3. Golden F St C. Problems of immersion. *British Journal of Hospital Medicine* 1980; **23:** 371–83.
4. Moritz AR. Chemical methods for determination of death by drowning. *Physiological Reviews* 1944; **24:** 70–88.
5. Editorial. Drowning and the diving reflex. *Canadian Medical Association Journal* 1973; **108:** 1209.
6. Fuller RH. The clinical pathology of human near-drowning. *Proceedings of the Royal Society of Medicine* 1963; **56:** 33–8.
7. Pearn JH. Secondary drowning in children. *British Medical Journal* 1980; **281:** 1103–5.
8. Kvittingen TD, Nass A. Recovery from drowning in fresh water. *British Medical Journal* 1963; **1:** 1315–7.
9. Siebke H Rd T, Brievik H, Lind B. Survival after 40 minutes submersion without cerebral sequelae. *Lancet* 1975; **1:** 1275–7.
10. Theilade D. The danger of fatal misjudgement in hypothermia after immersion. *Anaesthesia* 1977; **32:** 889–92.
11. Althaus U, Aeberlard P, Schupback P, Nachbur BH, Muhlemann W. Management of profound accidental hypothermia with cardiorespiratory arrest. *Annals of Surgery* 1982; **195:** 492–5.
12. Calderwood HW, Modell JW, Ruiz BC. The ineffectiveness of steroid therapy for treatment of fresh water near drowning. *Anesthesiology* 1975; **43:** 642–50.
13. Modell JH, Graves SA, Ketover A. Clinical course of 91 consecutive near drowning victims. *Chest* 1976; **70:** 231–8.
14. Grausz H, Amend WJC, Earley LE. Acute renal failure complicating submersion in sea water. *Journal of American Medical Association* 1971; **217:** 207–9.
15. Conn AW, Edmonds JF, Barker GA. Cerebral resuscitation in near drowning. *Paediatric Clinics of North America* 1979; **26:** 691–701.
16. Conn AW, Barker GA. Fresh water drowning and near drowning—an update. *Canadian Anaesthetic Society Journal* 1984; **31:** S38–44.
17. Beach Safety 1985. Produced by Advisory Committee on Beach Life Saving for Devon and Cornwall.

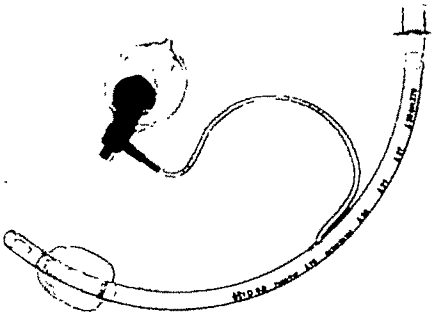
Mallinckrodt®
Critical Care

. . . your partner for advanced disposables synonymous with quality

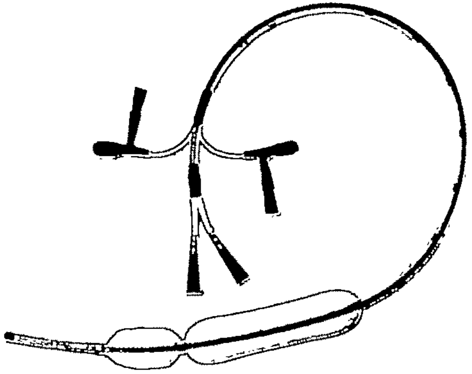
Anaesthesia



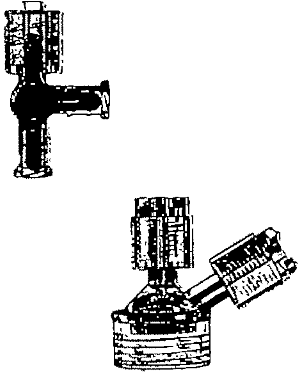
Intensive Care



Gastroenterology and Surgery



Invasive Monitoring



Our representative in your area will gladly advise you.

Mallinckrodt®
Critical Care

Mallinckrodt (U. K.) Ltd.
Critical Care Division
11 North Portway Close
Northampton
NN3 4RQ

Tel.: 0604-46132
Telex: 311 165 CHACOM G MALLUK

Association of Anaesthetists of Great Britain and Ireland

APPEAL FOR £600,000

for

REFURBISHMENT and FURNITURE

The response has now exceeded £400,000
Visit *your* headquarters to see progress.
Ensure *your* name is in the book of donors.

This Appeal will close on 31 December 1986
or earlier when the target is achieved.

Telephone
01–631 1650

9 Bedford Square,
London, WC1B 3RA

Anaesthesia, 1986, Volume 41, pages 649–681

Correspondence

Spinal anaesthesia and day care surgery? 650

P.R. Bromage, FFARCS, FRCP(C)

J.A. Lee, FFARCS and R.S. Atkinson, FFARCS 650

H. Flaatten, MD 651

Safer obstetric anaesthesia—just an ideal? 651

D.G. Moir, MD, FFARCS, DRCOG

Resuscitation on labour wards 651

D.G. Gaylard, BSc, FFARCS and I. Wilson, FFARCS

J. Selwyn Crawford, FFARCS, FRCOG 652

Anaesthesia for Caesarean section: no need for nightmares 652

Felicity Reynolds, MD, FFARCS

Possible subarachnoid migration of an epidural catheter 653

Deborah C. Phillips, FFARCS, Rosemary MacDonald, PhD, FFARCS and G. Lyons, FFARCS

Migration of epidural catheters 654

S.G. Webster, FFARCS

Epidural test dose in obstetrics 654

G.D. Prince, FFARCS, D.G. McGregor, FFARCS

Antibody involvement in reactions to neuromuscular blocking drugs 655

J. Watkins, PhD

Allergic drug reactions during anaesthesia 656

D.A. Moneret-Vautrin, MD and M.C. Laxenaire, MD

Paradoxical air embolism during neurosurgery 656

S. Roth, MD and DB Gould, MD

P.M. Brodrick, FFARCS, D. Jewkes, FFARCS, D. Coleman, FFARCS and S. Ingram, FFARCS 657

A.C. Thurlow, FFARCS 658

Awareness in paediatric anaesthesia 658

R.W. Okell, FFARCS

G.W. Black, MD, FRCPI, FFARCS and T.M. Gallagher, MD, MRCPI, FFARCSI 659

Anaesthesia for extracorporeal shock wave lithotripsy 660

J.D. Young, FFARCS

M.A. Abbott, FFARCS, J.R. Samuel, FFARCS and D.R. Webb, FRACS 660

Carbon dioxide elimination during apnoea 661

J.F. Stubbing, DRCOG, and J.R.D. Laycock, MSc, FFARCS

Acupressure and postoperative vomiting 661

E.N.S. Fry, FFARCS

Aortic knuckle and tracheal obstruction 662

G.S. Sarate, MD and S.M. Sant, MD

D.J. Sapsford, MB, BS, S.L. Snowdon, FFARCS and G.H. Whitehouse, FRCP, FRCR 662

Anaesthesia in idiopathic autonomic dysfunction 663

R.C. Hutchinson, FFARCS

B. Sweeney, FFARCS, S. Jones, MB, BS, and R.M. Langford, MB, BS, MRCP 663

Difficult intubation 664

A.S. Nathan, FFARCS, J.G. Scott, FFARCS and M. Mohandas, MB, BS

Intermittent mandatory ventilation for children 665

A.D. Crew, DRCOG, FFARCS, I.C. Grant, BA, FFARCS and M. Ward

Continuous infusions with vascular monitoring 665

B.J. Pollard, FFARCS

Vecuronium in the myasthenic patent 666

J.B. Eisenkraft, MRCP, FFARCS, R.K. Sawhney, MD and A.E. Papatestas, MD

Jennifer M. Hunter, FFARCS 667

Malignant hyperpyrexia susceptibility and childbirth 668

D.J.A. Rose, FFARCS

Unusual cause of obstructed airway in a child 000

L.R. McNicol, FFARCS

Transdermal glyceryl trinitrate 000

P. Charters, MD, MRCP, FFARCS

All correspondence should be addressed to Dr J.N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

Letters must be typewritten on one side of the paper and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters contained in 'Notice to Contributors' to *Anaesthesia* printed at the back of each issue. The degrees and diplomas of each author must be given in a covering letter.

Correspondence presented in any other style or format may be the subject of considerable delay and may be returned to the author for revision.

Overdose of intrathecal morphine 670
S.P. Pomonis, MD
Distress caused by urethral catheters 670
M.B. Coates, FFARCS
An airtight seal between facemask and beard 670
A.J. Mortimer, DRCOG, FFARCS
Alarming disconnexions 671
C.M.S. Cooper, MB, BS
The price of safety—cash too? 671
A. Gilston, FFARCS
Design of castors of anaesthetic machines 672
A.J. Munley, PhD and A. Shaw, BSc, C Eng.
High halothane concentrations from reversed flow in a vaporizer 672
R. Railton, PhD, F. Inst. P, C. Eng and M.D. Inglis, FFARCS
Hazardous tracheal tube pilot balloons 673
I.H. Herrema, MB, BCh
Disconnexion within an anaesthetic machine 674
H.M. Jones, MB, ChB and M.J. Sik, MA, PhD
Flowmeters: an old problem reappears 675
W. Richardson, BSc, C. Eng, MIMechE, and A. Shaw, BSc, C Eng, MIMechE
Protective sheath for nasotracheal tube 675
E. Cardan, MD and J. Vlad, MD
Peripheral circulation 676
C.M. Wait, BM, BCh
Anaesthesia by telephone: an aid to induction of anaesthesia in children 676
A.P. Boezaart, MB, ChB, DA, and C.H. Van Hasselt, FFARCS
The anaesthetic pacifier for induction of anaesthesia 677
K.A. Payne, FFARCS
Pneumothorax following insertion of a nasogastric tube 678
W.H. Konarzewksi, FFARCS, G.D.H. Richards, MB, BS and S.J. Thomson, MB, BS
The Bridgend modification of the Manley ventilator 679
J.Y. Kwan, DA, and R.W. Morris, FFARCS
The case for dilution of ketamine 680
M.K. Gademsetty, FFARCS
The Afya anaesthetic system 680
F.N. Prior, FFARCS
A.M. Brooks, FFARCS and J.M. Mecklenburgh. MSc 680
A resuscitation box for every anaesthetist? 681
P.A. Oakley, MA, MB, BChir, MRCGP and M. O'Connor, FFARCS
P.J. Hilton, FFARCS 681

Spinal anaesthesia and day care surgery?

Your editorial (*Anaesthesia* 1985; **40**: 1059–60) is refreshingly iconoclastic and cheering to those who welcome change for the good. But why subarachnoid block? Is it not better to leave the dura intact and not to have the worry of headaches? Day case management of herniae and operations of similar magnitude is clearly appropriate wherever cost means anything to anybody. By the same token, it is also appropriate to choose anaesthetic techniques which will keep the patient on his feet and reduce the chances of incidental morbidity and return visits to hospital.

It has been my practice to use epidural lignocaine (with adrenaline) for the actual surgery of hernia repair. An ilio-inguinal block is given in the recovery room, using 0.25% bupivacaine (with adrenaline) for prolonged postoperative pain relief. A loading dose of 1000 mg diflunisal (Dolobid) is given by mouth and the patient is sent home under escort by a friend or significant other to spend a pleasant, lazy and pain-free day away from dangerous mechanical devices such as chain-saws or motor cars. Diflunisal 500 mg is taken twice daily for 48–72 hours if required. Those of sterner stuff can return to non-hazardous and non-strenuous work the same day. One colleague of such disposition was found doing ward rounds on the evening of operation and again the next morning, without complaint and standing proudly as he went about his task. Clearly, epidural technique should be impeccable, since one should not encourage large accidental dural taps in ambulant patients.

Department of Anaesthesia, P.R. Bromage
King Khalid University Hospital,
P.O. Box 7805,
Riyadh, 11472,
Kingdom of Saudi Arabia

A reply

Thank you for allowing us to see the interesting letter written by Professor Bromage. We entirely take his point that extradural block has at least one great advantage over intradural, namely that it never causes postoperative headache (provided that the dura is not accidentally punctured). We would not dissent from his suggestion that if central neural blockade is to be given to a day stay patient, then the extradural approach is probably superior to the intradural. We are, of course, impressed by his practical method of management of such cases as shown by the splendid postoperative experience of one of his colleagues.

Our editorial was, however, written as a commentary on an article on intradural spinal analgesia in day stay surgery (*Anaesthesia* 1985; **40**: 1059–60) and we suggested that perhaps an overnight stay is not always necessary after this method of pain relief is employed.

Even less should it be necessary if extradural analgesia is used in patients considered suitable.

Southend Hospital,
Westcliff on Sea,
Essex, SS0 0RY

J.A. Lee
R.S. Atkinson

Another reply

Dr Bromage raises the question, why not epidural anaesthesia for day care surgery? Epidural anaesthesia is an excellent technique, and certainly so when the surgical procedure takes a long time.

We had to choose between general and regional anaesthesia for a short procedure, because the surgeon did not want to perform this under infiltration anaesthesia (*Anaesthesia* 1985; **40:** 1108–10). In our hands, subarachnoid block with lignocaine 5% has a 4–5 times faster onset time than epidural block with lignocaine 1%. We get the impression that spinal anaesthesia is more reliable, with less tendency to cause incomplete blocks or missed segments. The choice thus fell on spinal anaesthesia, since we wished to avoid general anaesthesia.

We also question the use of spinal anaesthesia, especially in young patients, since data from our department indicate a high frequency of postspinal headache in young patients in hospital. Eighteen of the 77 male patients between 20 and 30 years of age who had a spinal anaesthetic through a 25-G needle, developed signs of postspinal headache. The same happened to 16 out of 26 female patients (61.5%) in the same age group. These findings support the statement that it is not the ambulation, but the spinal anaesthetic itself, which makes it unsuitable in young patients.

Department of Anaesthesiology,
5016 Haukeland Hospital,
Bergen,
Norway

H. Flaatten

Safer obstetric anaesthesia—just an ideal?

The letter by Dr Ramamoorthy (*Anaesthesia* 1986; **41:** 82) is pertinent, timely and a cause for concern. Dr Ramamoorthy emphasises that all is not well in the everyday practice of obstetric anaesthesia. Competent assistance is not always available to the anaesthetist for the performance of cricoid pressure and other potentially life-saving procedures and sometimes there is no appropriate regimen directed towards the promotion of a safe gastric pH at the induction of anaesthesia. A further cause for concern is the prejudice of, it is to be hoped, a diminishing number of obstetricians against the use of a left lateral tilt.

Failure to provide skilled assistance, functional apparatus and an appropriate antacid regimen is not the fault of the junior anaesthetist. Where deficiencies exist, the consultant anaesthetists should act in order to rectify them.

Members of the Obstetric Anaesthetists' Association (OAA) will share Dr Ramamoorthy's concern and some may be surprised that such deficiencies exist in the United Kingdom in 1986. Several surveys, some of them recent, have investigated the anaesthetic staffing of maternity units and recommendations have been made by the OAA and other bodies. There have been few enquiries into the implementation of clinical practices designed to make anaesthesia safer. Office bearers of the OAA have discussed such a survey and Dr Ramamoorthy may be heartened to know that he is not alone in this concern.

The Queen Mother's Hospital,
Yorkhill,
Glasgow G3 8SH

D.G. Moir
President,
Obstetric Anaesthetists' Association

Resuscitation on labour wards

We read with interest Dr Crawford's comprehensive review of complications resulting from epidural analgesia for labour, (*Anaesthesia* 1985; **40:** 1219–25). The possibility of subarachnoid injection of local anaesthetic during a top up is a rare, but potentially fatal complication, and we agree that staff competent in resuscitation must always be immediately available.

However, even in obstetric units with a resident anaesthetist, a problem may arise following an epidural top up by a midwife, when the anaesthetist is committed elsewhere (emergency Caesarean section, for example). The obstetric medical staff may well then be called on to initiate resuscitation until the anaesthetist is available.

The standard of basic resuscitation skills possessed by most hospital doctors has been a subject of recent report[1] and discussion,[2,3] and we would suggest that instruction in resuscitation techniques for obstetric medical staff in particular is now essential if occasional disasters are to be avoided.

Plymouth General Hospital,
Plymouth PL4 8QQ

D.G. Gaylard
I. Wilson

References

1. Skinner DV, Camm AJ, Miles S. Cardiopulmonary resuscitation skills of preregistration house officers. *British Medical Journal* 1985; **290:** 1549–50.

2. Baskett PJF. Resuscitation needed for the curriculum? *British Medical Journal* 1985; **290:** 1531–2.
3. Barcroft J. Resuscitation skills. *Anaesthesia* 1985; **40:** 1015–6.

A reply

I am totally in agreement with the views expressed by your correspondents. However, such a back-up facility must not encourage a dilution or reduction of intensity of supervision to below acceptable standards by the anaesthetists involved in the service.

J. Selwyn Crawford
The Birmingham Maternity Hospital,
Edgbaston, Birmingham B15 2TG

Anaesthesia for Caesarean section: no need for nightmares

It was distressing to learn from the media that there are still many women who suffer awareness under general anaesthesia for Caesarean section, and that there are still reputable anaesthetists who will defend the practice of skimping on anaesthesia in the belief that this is in the interests of the baby—this despite repeated warnings of the dangers of amnesic wakefulness[1] and even awareness[2] during Caesarean section.

It is essential to distinguish between asphyxia, which can do permanent damage to the baby's brain, and anaesthesia, which is a reversible process. Since neonatal intubation and artificial ventilation became widespread in the 1960s, minor degrees of transient neonatal depression should pose no threat to cerebral oxygenation. True, maternal anoxia and major circulatory depression would impair fetal oxygenation, but these are *not* the inevitable accompaniment of modern anaesthesia, in the wedged position, using *adequate* though not excessive doses of anaesthetic agents. However, maternal stress resulting from awareness, *is* likely to reduce maternal placental blood supply.

Anaesthetic agents, with the exception of neuromuscular blocking drugs, all cross the placenta readily, but they can only accumulate slowly in the baby, simply because, as may sound obvious but is frequently forgotten, maternal blood does not perfuse the baby's brain! Thus, the bolus effect of thiopentone cannot be reproduced in the fetus,[3,4] and though umbilical *venous* concentrations may be high, this is only the blood that is directly downstream of the placenta, and not that which perfuses the fetal brain. Even nitrous oxide, though freely diffusible and much less tissue-concentrated than thiopentone, may take the best part of an hour to achieve materno-fetal equilibration.[5] The safety of enflurane in the field is widely attested, but like nitrous oxide it may accumulate briefly. Modest haste is therefore the order of the day for the surgery prior to delivery, rather than mingy anaesthesia.

Does anaesthesia pose a greater threat to the compromised fetus? Placental transfer rates, and hence fetal dose, of freely diffusible compounds, are dependent upon umbilical flow[6] which is *reduced* in fetal distress. Moreover, surgery is always swift in such circumstances. It is the fit baby delivered by leisurely surgery that will suffer drug effects, not the compromised fetus.

In the past it has been prolonged treatment of the mother with barbiturates and benzodiazepines that has had a lasting detrimental effect in the neonate,[7,8] not correctly conducted anaesthesia for a brief period. It cannot be in the best interests of any baby to be born to a mother who suffers nightmares at the memory of his birth.

When I questioned the value of routine antacid prophylaxis in labour,[9] I headed my letter 'a sacred cow under attack'. The only outcome was a spate of reprint requests from vets. I hope the present letter heading will attract the attention of a more relevant sector of the population.

Anaesthetic Unit, Felicity Reynolds
St Thomas's Hospital Medical School,
London SE1 7EH

References

1. Tunstall ME. The reduction of amnesic wakefulness during Caesarean section. *Anaesthesia* 1979; **34:** 316–9.
2. Editorial. On being aware. *British Journal of Anaesthesia* 1979; **51:** 711–2.
3. Reynolds F. Drug transfer across the placenta. In: Chamberlain G, Wilkinson A, eds. *Placental transfer.* Tunbridge Wells: Pitman Medical, 1979: 166–81.
4. Wylie WD, Churchill Davidson H. *A practice of anaesthesia,* 5th edn. London: Lloyd-Luke, 1984: 1070.
5. Stenger VG, Blechner JN, Prystowsky H. A study of prolongation of obstetric anesthesia. *American Journal of Obstetrics and Gynecology* 1969; **103:** 901–7.
6. Hamshaw-Thomas A, Reynolds F. Placental transfer of bupivacaine, pethidine and lignocaine in the rabbit. Effect of umbilical flow rate and protein content. *British Journal of Obstetrics and Gynaecology* 1985; **92:** 706–13.
7. Brazelton TB. Psychophysiologic reactions in the neonate II. Effect of maternal medication on the neonate and his behaviour. *Journal of Pediatrics* 1961; **58:** 513–8.
8. Cree JE, Meyer J, Hailey DM. Diazepam in labour: its metabolism and effect on clinical condition and thermogenesis of the newborn. *British Medical Journal* 1973; **4:** 251–5.
9. Reynolds F. Antacids and maternal death: a sacred cow under attack. *Anaesthesia* 1983; **38:** 391–2(*c*).

Possible subarachnoid migration of an epidural catheter

We would like to report a case of concealed dural tap which occurred during our current study of epidural catheter migration during labour.

The patient, a 21-year-old primigravida with a history of chronic mastoid disease and scheduled for further ear surgery, was given epidural analgesia as pain relief for labour. The $L_{2/3}$ interspace was chosen and the epidural space was easily identified at 3.5 cm depth using loss of resistance to saline; further confirmation was obtained using a fresh, air-filled 2-ml syringe. The epidural catheter was then threaded through the Tuohy needle in the normal way and adjusted to leave 3 cm in the epidural space. A test dose of 4 ml 1% plain lignocaine, given while the patient was still lying on her left side, produced neither sensory, motor nor sympathetic signs or symptoms and 5 minutes later she was given 7 ml 0.5% plain bupivacaine in the sitting position. Analgesia was achieved over the next 5–10 minutes. Her blood pressure decreased from a pre-epidural level of 120/70 to 100/60 mmHg at 15 minutes and 90/60 mmHg at 30 minutes.

The sensory blockade was tested to pin-prink at 30 minutes and found to extend bilaterally to the T_8 dermatome. Modified motor power in the legs and toes was maintained throughout and the patient was happy. A live infant was born by spontaneous vertex delivery before the administration of a further top-up; the effects of the epidural had been allowed to wear off, since the mother expressed a desire to be able to feel the delivery.

The epidural catheter was removed after delivery; the distance from the skin to the 10-cm mark was recorded as part of our study on epidural catheter migration during labour.

On routine follow-up the next morning she complained of a headache with similar features to those she experienced from her mastoid. The headache became more severe later the same morning and when she was seen again she had a more typical spinal headache with nausea, neck stiffness and photophobia. A diagnosis of concealed dural tap was considered, especially since, on closer questioning, she mentioned that she had had tingling hands during her labour after the epidural had been sited.

She was treated with analgesics, anti-emetics and bed rest and encouraged to lie prone, but her symptoms persisted with sufficient severity for us to perform an epidural blood patch the following morning. This proved effective for about 30 hours when she said her headache and nausea returned.

Three days after the blood patch she was offered the opportunity of another blood patch the following day if her symptoms had not improved. Features of the headache still seemed to be predominantly spinal in nature, but could not entirely be separated from those experienced as a result of her mastoid condition. She was therefore referred to the ENT department who reported that her ear was not responsible for her symptoms. On the day of the proposed second blood patch she was considerably improved and it was deferred. She maintained her improvement and was discharged home 8 days after her confinement.

From the record of the catheter siting and its removal, it was found that the catheter had migrated 2 cm into the patient so that 5 cm of catheter were in the epidural space. Our study into epidural catheter migration in labour is intended to find out how many catheters move from their original positions, in which direction they move relative to the patient, and what effects this movement has on the effectiveness of the epidural analgesia. Thus, we are able to state with some certainty, that the catheter in this case had migrated a significant distance into the patient.

There remains uncertainty about the moment at which the dural tap occurred. The catheter siting was performed with ease and at no time was free fluid seen to drip from either the needle or the catheter. It is possible that a small 'nick' was made in the dura that did not allow free leakage of cerebrospinal fluid (CSF) until the intradural pressure was raised by the expulsive efforts of delivery. The test dose of lignocaine produced no discernible effects and dural tap was not suspected. Straightening the patient from the flexed position adopted to allow access to the epidural space and sitting her up may have encouraged the inward migration of the catheter as it was gripped by the ligamentum flavum and this may have caused the dural puncture.

The effects of the bupivacaine did not raise any suspicions of dural tap although perhaps analgesic levels of T_8 are not common with a 7-ml dose given in the sitting position. It is also possible that only one of the three ports in the catheter lay intradurally, resulting in the bulk of the dose being given epidurally but allowing free leakage of CSF when the catheter was removed. The tingling of her hands did not correlate with the measured sensory level of the blockade and was not mentioned by the patient until the following day. No further bupivacaine was given, so features which might have suggested subarachnoid administration were not elicited.

Measurement of the length of catheter in the epidural space on siting and removal may provide corroborative evidence that a catheter puncture of the dura may have occurred. It seems reasonable to assume that catheter migration is most likely to occur when the patient is moved from one position to another. This could be at any time from the position used on siting the catheter to the position adopted for delivery and after, up until its removal. Perhaps more importance should be attached to the fixation of the catheter to prevent its migration into the epidural space as well as its migration out.

Clinical Sciences Building,
St James's Hospital,
Beckett Street,
Leeds LS9 7TF

DEBORAH C. PHILLIPS
ROSEMARY MACDONALD
G. LYONS

Migration of epidural catheters

The case report by Kumar, Dennison and Lawler (*Anaesthesia* 1985; **40:** 1100–2) illustrates the importance of correct placement of the epidural catheter in epidural analgesia. My personal experience also suggests that 3 cm is the ideal length of the Portex catheter (with side holes) to be inserted into the epidural space. The authors touch briefly on the problem of fixation of the catheter to the skin and the difficulty of depth estimation in the obese. This is quite important when only a short segment of the catheter is in the epidural space.

There is considerable movement of the skin and soft tissues over the lumbar spine with change of position in an obese patient. This can be readily observed if the patient is moved before a dressing is applied to the puncture site, since the epidural catheter is usually grasped reasonably firmly by the ligamentum flavum. In one patient whose epidural space was 12.5 cm from the skin, 2.5 cm of catheter was pulled in through the skin hole with change from the sitting to the left lateral position. If a fixative dressing had been applied in the sitting position, subsequent top ups would have been unsuccessful.

Consequently, my practice now in obese patients is to insert the epidural catheter and then change the patient's position before applying the fixative dressing (either sitting to left lateral, or left lateral to sitting). Consistent success with epidural analgesia depends on attention to detail.

Department of Anaesthesia,
King Edward Memorial Hospital for Women,
Subiaco,
Western Australia, 6008

S.G. WEBSTER

Epidural test dose in obstetrics

May we take issue with at least some of the points made by Dr Casey in his letter concerning the epidural test dose in obstetrics (*Anaesthesia* 1985; **40:** 597). The occurrence of deaths associated with epidural analgesia in obstetrics is clearly a matter of great concern.[1–4] The use of an effective epidural test dose would certainly result in a decrease in the number of accidental subarachnoid and intravenous injections of local anaesthetic, but to suggest that this procedure can ever be 100% effective is dangerous and fallacious. Differentiation between epidural and subarachnoid injection of small volumes of local anaesthetic is a particular problem in the parturient, whose judgement is often clouded by pain, panic and pethidine. The effect of an intrathecal injection of local anaesthetic is essentially similar to that produced by an epidural injection, since both cause elements of motor, sensory and autonomic block. Any differences which are detected depend on the interpretation of the degree of block produced by the test dose when compared with previous experience of injection of a similar dose into the epidural space. Subarachnoid injection in pregnancy causes a relatively high level of block compared to the nonpregnant patient, largely due to the alterations in epidural space pressure, on movement from the lateral to the supine position.[5,6] Russell has shown that this phenomenon results in an average extension of the block by six dermatomes when isobaric local anaesthetic is used for spinal anaesthesia for Caesarean section.[7] The patient who has an epidural test dose is not normally moved between the injection and its interpretation, so this effect will not occur. Thus, though high blocks have frequently been reported following deliberate spinal injection of 3–4 ml isobaric local anaesthetic,[8,9] there are, as yet, no reports of this happening after a properly conducted epidural catheter test dose. The corollary of this is that if a small volume of 5% lignocaine is injected with the patient in the sitting position, and the patient is not then moved, the resulting block, despite its density, could be confined to the sacral dermatomes. An additional problem is that an injection of even a small volume of such a concentrated solution of lignocaine into the epidural space could be expected rapidly to produce a limited epidural block. Surely the questions: 'How is this test dose to be administered?' and 'How, and when, is it to be interpreted?' must be precisely answered before one can even begin to determine whether massive intrathecal injections are truly avoidable using this test dose solution as Dr Casey implies. Personally, we doubt it. Somewhere, perhaps even now, an anaesthetist is attempting an epidural block on an hysterical mother-to-be who is breathing Entonox; together they ensure that total spinal blocks are here to stay.

Acceptance of the principle that occasional massive intrathecal injections may occur even when a test dose has been carefully administered, has considerable implications for the way in which obstetric epidural anaesthesia is practised in this country. We must insist that local anaesthetic is not injected through an epidural catheter unless a doctor competent in the skills of intubation and resuscitation is available at a minute's notice.

Department of Anaesthesia, G.D. Prince
Regional Cardiothoracic Centre, D.G. McGregor
Freeman Hospital,
Newcastle upon Tyne

References

1. Marx GF. Cardiotoxicity of local anesthetics—the plot thickens. *Anesthesiology* 1984; **60:** 3–5.
2. Abouleish E, Bourke D. Concerning the use and abuse of test doses for epidural anesthesia. *Anesthesiology* 1984; **61:** 344.
3. Winn D. How dangerous is the jab? *The Sunday Times.* 26th August, 1984: p. 35.
4. Timmins N. Pain free childbirth: How safe is it? *The Times.* 1st February, 1985; p. 11.
5. Shah JL. Effect of posture on extradural pressure. *British Journal of Anaesthesia* 1984; **56:** 1373–7.
6. Barclay DL, Renegar OJ, Nelson EW. The influence of inferior vena cava compression on the level of spinal anesthesia. *American Journal of Obstetrics and Gynecology* 1968; **101:** 792–800.
7. Russell IF. Spinal anaesthesia for Caesarean section. The use of 0.5 percent bupivacaine. *British Journal of Anaesthesia* 1983; **55:** 309–14.
8. Russell IF. Intrathecal bupivacaine 0.5 percent for Caesarean section. *Anaesthesia* 1982; **37:** 346–7.
9. Stonham J, Moss P. The optimal test dose for epidural anesthesia. *Anesthesiology* 1983; **58:** 389–90.

Antibody involvement in reactions to neuromuscular blocking drugs

Thank you for the opportunity to reply to the critical letter from Dr Baldo[1] about our own modest views[2] on allergic drug reactions. It was not the intention of the Sheffield group to denigrate the observations of this well respected Australian group, only to suggest caution to their wilder extremes of interpretation. One recalled, however, two lines from Hamlet: 'The lady doth protest too much, methinks' and 'Myself I am but indifferent honest'.

In general terms, the immunological problems of anaesthesia are analogous to those encountered in food allergies, but here are a few specific observations on the points raised by Dr Baldo.

An individual raises antibodies to the many antigens encountered daily as part of normal immunological defence.

Such defence has considerable advantage to the individual's wellbeing, unless he generates a grossly excessive (hypersensitivity) response. What evolutionary advantage pertains to the latter response is far from clear, but the antibodies produced are likely to be of IgE class and their formation already implies distinct genetic traits for that individual.

If IgE antibodies are widely produced to neuromuscular blocking drugs, we might expect patients with atopy, allergy or other evidence of IgE involvement to be particularly involved. Many first time reactors have extremely low or nonexistent plasma IgE levels.[3]

If the hazard is indeed the specific determinant (substituted ammonium group) implicated by Dr Baldo, why are not all neuromuscular drugs similarly (clinically) implicated?[4] If the answer invokes a particular molecular spatial arrangement, e.g. proximity to an aromatic ring, then surely this dilutes the significance of the presence of the specific determinant *per se*. We might ask, at an even more fundamental level, why such sensitised patients do not exhibit clinical allergy to their sensitising agents, be they foods, cosmetics or whatever?

Even the demonstration of circulatory specific antibodies *per se* does not define their role in the clinical reaction. A useful illustration here is of the cross-reacting antibodies to dextran. Such antibodies are often present in high titre in patients who have suffered pneumococcal infections, but their role in *all* dextran infusion reactions is highly equivocal.

Intradermal tests may be misleading. It is very easy to generate false positives and in our prospective trials[5] such tests provided no help whatsoever. It is surprising that Dr Baldo does not refer to this,[5] since it was presented at the Nancy Meeting which generated one of his own references!

Finally, I see no reason to believe that our caution means our advice to anaesthetists is more hazardous than that provided by our colleagues in Australia.

Department of Immunology, J. Watkins
Royal Hallamshire Hospital,
Sheffield S10 2RX

References

1. Baldo BA. Cross reactions of neuromuscular blocking drugs and anaphylactoid reactions. *Anaesthesia* 1986; **41:** 550.
2. Watkins J, Nimmo WS. 'Allergic' drug reactions during anaesthesia. *Anaesthesia* 1985; **40:** 813–4.
3. Lavery GG, Clarke RSJ, Watkins J. Histaminoid responses to atracurium, vecuronium and tubocurarine. *Annales Francaises d'Anésthésie et de Réanimation* 1985; **4:** 180–83.
4. Watkins J. Adverse anaesthetic reactions. An update from a proposed national reporting and advisory service. *Anaesthesia* 1985; **40:** 797–800.
5. Wood M, Watkins J, Wild G, Levy CJ, Harrington C. Skin testing in the investigation of reactions to intravenous anaesthetic drugs. A prospective trial of atracurium and tubocurarine. *Annales Francaises d' Anésthésie et de Réanimation* 1985; **4:** 176–9.

Allergic drug reactions during anaesthesia

We read with much interest the letter from Dr J. Watkins and Professor W. Nimmo (*Anaesthesia* 1985; **40**: 813–4) which expressed some reservations about cutaneous testing aimed at the diagnosis of adverse reactions to muscle relaxants.

They state that these substances have notorious skin histamine release characteristics, even at dilutions of 1:1000 or 1:10000 of the normal dosages and give the example of a recent study performed with atracurium and tubocurarine. Skin weals were observed, but subsequent clinical exposure to one of these drugs did not produce an adverse clinical response. They then conclude that skin testing is not a reliable method to detect anaphylaxis to muscle relaxants.[1]

We do not agree with this statement for several reasons. Firstly, atracurium and tubocurarine are the most histamine-releasing muscle relaxants, much more than alcuronium, suxamethonium, pancuronium or vecuronium. These two drugs are not used in France. Secondly, Watkins *et al.*, performed the tests on the anterior part of the forearm, while the other authors[2,3] injected drugs in the upper part of the back, or on the exterior part of the arm, where the histaminic reactivity is somewhat different. Thirdly, there is no complete correlation between the existence of specific IgEs and the occurrence of a clinical reaction. For instance, the risk of anaphylaxis in patients allergic to hymenoptera venom is about 40%. The absence of a clinical reaction cannot exclude the presence of specific IgE.

For the same reason, it is not cautious to discard intradermal testing in the search for crossed anaphylaxis, on the basis that clinical reactions of crossed anaphylaxis seem to be infrequent. In our experience, intradermal testing is useful for the diagnosis of anaphylaxis to suxamethonium, alcuronium, pancuronium or vecuronium.[3] The criteria for positive tests on the back is a diameter of the weal no less than 10 mm, when 0.05 ml of the dilution 1/1000 is injected. The size of the erythema is not a significant variable. A smaller diameter weal may indicate a nonspecific histaminic reaction. The use of a scale of dilutions may help to differentiate the two possibilities, as we showed in six cases of anaphylaxis to one muscle relaxant, which were tested to atracurium: five patients had a histaminic reaction with the dilution 1:10 and one obviously had a crossed anaphylaxis, the test being positive at 1:1000.[4] The positive intradermal reactions are well correlated with a positive human basophil degranulation test and, more recently, a radio-immunoassay according to a technique which has been published by Baldo.[5,6]

D.A. Moneret-Vautrin
Service de Medecine D. Immuno-allegologie
Hopital de Brabois,
54511 Vandoeuvre,
France

M.C. Laxenaire
Departement d'Anesthesiologie,
Hopital central,
Nancy, France

References

1. Lavery GG, Clarke RSJ, Watkins J. Histaminoid responses to atracurium, vecuronium and tubocurarine. *Annales françaises d'anésthesie et de réanimation* 1985; **4**: 180–3.
2. Fisher MM. Skin testing in the preoperative diagnosis of anaesthetic allergy. *Annales Françaises l'Anesthesie et de Réanimation* 1985; **4**: 192–4.
3. Moneret-Vautrin DA, Mouton C, Widmer S. Anaphylaxis to muscle relaxants. Predictive value of intradermal tests and study of crossed anaphylaxis. *Annales françaises d'Anesthésie et de Reánimation* 1985; 4: 186–91.
4. Laxenaire MC, Moneret-Vautrin DA, Widmer S. The histamine and anaphylactic risks due to atracurium. *Annales Francaises d'Anesthesie et de Réanimation* 1985; **4**: 495–9.
5. Baldo BA, Fisher MM. Anaphylaxis to muscle relaxant drugs: cross-reactivity and molecular basis of binding of IgE antibodies detected by radioimmunoassay. *Molecular Immunology* 1983; **20**: 1393–400.
6. Baldo BA, Fisher MM. Substituted ammonium ions as allergenic determinants in drug allergy. *Nature* 1983; **306**: 262–4.

Paradoxical air embolism during neurosurgery

In their article (*Anaesthesia* 1985; **40**: 981–9), Dr Clayton and colleagues present four case histories of severe haemodynamic changes resulting from the complication of entrained air. All four patients were monitored with a capnograph and changes in end tidal CO_2 preceded the haemodynamic sequelae in each case. None of the patients was monitored with a precordial Doppler or central venous catheter, which could have afforded earlier diagnosis and therapy. The omission of these techniques in the four cases warrants further discussion.

The precordial Doppler has been cited as the most sensitive and reliable indicator of air embolism.[1–4] In one large retrospective study of 382 patients in the sitting position for neurosurgery,[5] changes in the precordial Doppler were the first sign of air embolism in 20 out of 22 patients (91%). Two patients had no change in Doppler sounds but did have evidence of air embolism by changes in end tidal CO_2 and aspiration of air from a right atrial catheter. It is acknowledged that the Doppler may record clinically insignificant episodes of entrained air, but awareness of even these small amounts are significant as an abrupt bolus infusion may occur.[6] Slow absorption of air in the pulmonary vascular system may lead to ventilation–perfusion mismatching and postoperative pulmonary complications.[6] Clayton and colleagues agree that the Doppler may detect quantities of air not detectable by the capnograph; they fail to explain why this is not routine monitoring in their patients. It is possible that the use of the Doppler could have prevented occurrence of the paradoxical air emboli by prompting both surgeon and anaesthetist to commence therapy earlier, for example, flooding of the surgical site, use of bone wax, jugular venous compression or withdrawal of nitrous oxide.

The authors cite a reference[6] which claims their value as equivocal about the use of central venous catheters. In cases of abrupt aspiration of large volumes of air, as in these four cases, the catheter is potentially life-saving. In addition, considering the low complication rate of central venous catheterisation in skilled hands and the rare but devastating complication of paradoxical air embolisation, many authorities feel its use is indicated routinely.[7]

In summary, we believe that use of the combination of central venous catheterisation, precordial Doppler, and end tidal CO_2 are indicated for sitting position neurosurgery and could possibly have prevented the disastrous complications reported by Clayton and colleagues.

Division of Anesthesiology,
Cleveland Clinic Foundation,
9500 Euclid Avenue,
Cleveland, Ohio 44106, USA.

S. Roth
D.B. Gould

References

1. Brechner TM, Brechner VL. An audible alarm for monitoring air embolism during neurosurgery. *Journal of Neurosurgery* 1977; **47**: 201–4.
2. Buckland RW, Manners JM. Venous air embolism during neurosurgery. A comparison of various methods of detection in man. *Anaesthesia* 1976; **31**: 633–43.
3. Edmonds-Seal J, Prys-Roberts C, Adams AP. Air embolism. A comparison of various methods of detection. *Anaesthesia* 1971; **26**: 202–8.
4. Gildenberg PL, O'Brien RP, Britt WJ, Frost EAM. The efficacy of Doppler monitoring for the detection of venous air embolism. *Journal of Neurosurgery* 1981; **54**: 75–8.
5. Standefer M, Bay JW, Trusso R. The sitting position in neurosurgery: a retrospective analysis of 488 cases. *Neurosurgery* 1984; **14**: 649–58.
6. Frost EAM. Some inquiries in neuroanaesthesia and neurological supportive care. *Journal of Neurosurgery* 1984; **60**: 673–86.
7. Michenfelder JD (Editorial). Central venous catheters in the management of air embolism whether as well as where. *Anesthesiology* 1981; **55**: 339–41.

We read with interest the article by Clayton *et al.* and would like to comment on two points.

Firstly, the Doppler ultrasonic air embolism detector is no more than a detector, used on its own; it will not reduce the incidence of air embolism, it can only increase the detection rate. It also suffers from a major drawback, in that it is very susceptible to electrical interference in the operating theatre and, critically, its signal is cut out when diathermy is most needed. It is likely that the diathermy will be in use at the moment when an air embolism is likely to occur, such as during division of muscle and fascial layers. Our policy is to use the Doppler in conjunction with an infrared end tidal carbon dioxide monitor, to minimise the time lost in the detection of an air embolism.

Secondly, no preventive measures appear to have been taken against the possibility of an air embolism, in any of the patients reported in the article. It appears strange that when placing a patient in the sitting position and risking an air embolism, that positive steps were not taken to raise the venous pressure prior to surgery. After all, if the venous pressure is high, then an air embolism cannot take place and the problem of paradoxical air embolism need not arise. The use of positive end expiratory pressure and an antigravity suit have been described in the past as effective methods of raising the venous and arterial pressures, so perhaps we should place more emphasis on prophylaxis rather than on treatment.[1] It is also interesting to note that in no patient was a right atrial catheter inserted prior to surgery. Several workers[2–4] have recommended the use of a right atrial catheter as a means of detection and treatment of air embolism, for cases such as these. 'The potential to recover embolised air via a catheter should not be abandoned'.[3] Indeed, the author whose reference is quoted as indicating that the use of a right atrial catheter is unnecessary, accepts that in some circumstances it is strongly recommended (arteriovenous malformations, tumours involving sinuses).[5] Albin, in a series of patients, had a 75% success rate in aspirating air from patients who had entrained air detected by a Doppler.[6] Whilst appreciating the problems involved in the accurate placement of a right atrial catheter, the ability to remove air should not be dismissed lightly.

The National Hospital for
Nervous Diseases,
Queen's Square,
London WC1N 3BG

P.M. Brodrick
D. Jewkes
D. Coleman
S. Ingram

References

1. Hewer AJH, Logue V. Methods of increasing safety of neuroanaesthesia in the sitting position. *Anaesthesia* 1962; **17**: 476–81.
2. Albin MS, Chang JL, Brabinski M, Waterman P, Maivald P, Paulter S. Intracardiac catheters in neurosurgical anesthesia. *Anesthesiology* 1979; **50**: 67–9.
3. Michenfelder JF. Central venous catheters in the management of air embolism; whether as well as where. *Anesthesiology* 1981; **55**: 339–41.

4. Munson ES. Intracardiac catheters in neurosurgical anesthesia. *Anesthesiology* 1979; **50:** 67.
5. Frost EAM. Some inquiries in neuroanesthesia and neurological supportive care. *Journal of Neurosurgery* 1984; **60:** 673–86.
6. Albin MS, Babinski M, Maroon JC, Jannetta PJ. Anesthetic management of posterior fossa surgery in the sitting position. *Acta Anaesthesiologica Scandinavica* 1976; **20:** 117–28.

A reply

It is, in my opinion, naive of Dr Roth and Dr Gould to believe that routine Doppler monitoring and placement of central venous catheters can prevent paradoxical embolism during neurosurgery in the sitting position.

We did state in our article that a reliable Doppler monitor, which is easily positioned and can record in the presence of diathermy interference, should be used. However, British neuroanaesthetists have been less impressed with the efficacy of existing monitors than their American colleagues. This may relate to the different use of surgical diathermy in the two countries. British neurosurgeons use diathermy almost continuously when opening a craniotomy. This obliterates the Doppler signal on current machines and leaves radio silence during the time of maximum risk of air embolism. In addition, the subjective and nonquantitative aspects of Doppler monitoring are less than ideal. Thus, in a British operating theatre, the Doppler monitor, although theoretically the most sensitive indicator, has often proved an unreliable detector of air embolism. Newer techniques of Doppler monitoring may improve the situation as we mentioned in our article.[1]

Dr Roth and Dr Gould seem to have missed one of the main points of our article, namely central venous catheterisation. It may be useful in air lock of the right heart following bolus aspiration of large volumes of air. We consider that this is a rare event in neurosurgery and the common clinical situation is slow entrainment of smaller volumes of air over a longer period which can have devastating effects in the coronary or cerebral circulations. This is why several authors[2,3] have noted that aspiration of air from the right atrium is often difficult and does not lead to an improvement in circulatory status.

Michenfelder,[4] in a recent review, states that 10 percent of all patients undergoing neurosurgery in the sitting position have the combination of a probe-patent foramen ovale and venous air embolism. He estimates that in one third of this group, there is a right-to-left pressure gradient and that the potential for paradoxical embolism exists. The use of transeosophageal echocardiography and other noninvasive techniques may eventually allow this high risk group to identified. However, as several workers have demonstrated,[5,6] a venous air entrainment rate of more than 0.15–0.30 ml/kg/minute may allow air to cross into the arterial system by the transpulmonary route without any anatomical cardiac defects.

The anaesthetists at the National Hospital have always been great believers in the prophylactic effect of raising venous pressure, but the argument does not stand up to critical analysis. One of the main reasons for surgeons using the sitting position is the excellent operating conditions produced. The raising of venous pressure, by either the antigravity suit or the use of positive end expiratory pressure will nullify these conditions by raising intracranial pressure and causing increased bleeding. It would seem simpler not to have used the sitting position in the first place. In addition, the use of PEEP or an antigravity suit, by increasing right atrial pressure, will make paradoxical embolism much more likely if venous air embolism does occur.

It does appear, at the moment, that the only way to prevent paradoxical embolism in neurosurgery is to abandon the sitting position.

St George's Hospital,
London SW17
A.C. Thurlow

References

1. Martin RW, Colley PS. Evaluation of transoesophageal Doppler detection of air embolism in dogs. *Anesthesiology* 1983; **58:** 117–23.
2. Bedford RF, Marshall WK, Butler A, Welsh JE. Cardiac catheters for diagnosis and treatment of venous air embolism. A prospective study in man. *Journal of Neurosurgery* 1981; **55:** 610–4.
3. Edmonds-Seal J, Prys-Roberts C, Adams AP. Air embolism. A comparison of various methods of detection. *Anaesthesia* 1971; **26:** 202–8.
4. Michenfelder J. Cerebral emboli of paradoxical origin. *Intelligence Reports in Anaesthesia* 1984; **1:** 10–1.
5. Spencer HP, Oyama T. Pulmonary capacity for dissipation of venous gas emboli. *Aerospace Medicine* 1971; **42:** 822–7.
6. Butler BD, Hills BA. Transpulmonary passage of venous air emboli. *Journal of Applied Physiology* 1985; **59:** 543–7.

Awareness in paediatric anaesthesia

The paper by Dr Gallagher and Dr Black (*Anaesthesia* 1985; **40:** 1073–7) contains interesting information on the uptake of volatile agents in children. However, in attempting to collect their data in the absence of confounding factors, the authors may have risked awareness under anaesthesia in some of the children studied.

Awareness under anaesthesia is difficult to study in children but is, nevertheless, documented[1] and may be more common than in adults.[2] The precise end tidal levels of volatile anaesthetic agents which are necessary to prevent awareness in children are not known, nor would studies to establish them be readily acceptable to the patients or their parents. Minimum alveolar concentration (MAC) values for halothane have been studied in children and have been found to be higher than those for adults. Gregory, Eger and Munson[3] found MAC values for halothane ranging from 1.08 in neonates to 0.87 at an average age of 8.4 years as compared with 0.75 in adults. It can be anticipated that MAC values for other volatile agents are correspondingly higher in children. Eger[4] has suggested that 0.6 MAC represents MAC awake, a level at which 50% of patients open their eyes and respond to simple commands, and thus confirm awareness of their surroundings.

The patients under study were induced with thiopentone 5 mg/kg and paralysed with pancuronium 0.1 mg/kg. Healthy, unpremedicated children could not be expected to remain anaesthetised for longer than 5 minutes on this dosage of thiopentone. Following induction, the patients' lungs were ventilated with 100% oxygen until stable end tidal carbon dioxide levels were achieved (while not apparent from the paper as published, this was noted during the presentation at the Annual Scientific Meeting, 1984). Subsequently, volatile agents were introduced at an inspired concentration of 1.0%. End tidal values corresponding to 0.6 adult MAC, though not necessarily 0.6 patient MAC were achieved within one minute of vapour introduction for all groups receiving methoxyflurane and within 5 minutes for all halothane groups. In contrast, 0.6 adult MAC was not achieved until 10 minutes in the isoflurane groups, while in the enflurane groups this value was never achieved within the 30 minutes of the study. It should be noted that an inspired concentration of 1.0% represents 6.25 adult MAC for methoxyflurane, but only 0.6 adult MAC for enflurane.

It would be interesting to know if any of the children studied indicated that they were aware of paralysis and controlled ventilation, either in response to specific enquiry, or voluntarily. Information of this kind might prove useful in selecting appropriate concentrations of volatile agents in paediatric practice, if, as with these patients, it is planned to use neither premedication nor intravenous supplements.

Department of Anaesthesia, R.W. OKELL
Broadgreen Hospital,
Thomas Drive,
Liverpool L14 3LB

References

1. MCKIE BD, THORP EA. Awareness and dreaming during anaesthesia in a paediatric hospital. *Anaesthesia and Intensive Care* 1973; **1**: 407–14.
2. UTTING JE. Awareness during surgical operations. In: ATKINSON RS, LANGTON HEWER C, eds. *Recent advances in anaesthesia and analgesia.* London: Churchill Livingstone, 1982: 115–6.
3. GREGORY GA, EGER EI II, MUNSON ES. The relationship between age and halothane requirements in man. *Anesthesiology* 1969; **30**: 488–91.
4. EGER EI II. *Anesthetic uptake and action.* Baltimore: Williams and Wilkins Co., 1974.

A reply

Dr Okell comments that some of the children may have been aware of their surroundings during anaesthesia.

In devising a protocol for an investigation of this nature, it is important to exclude as many complicating factors as possible in order to obtain meaningful data. We indicated in the paper that it was considered necessary to ensure that end tidal carbon dioxide concentrations were within normal limits following thiopentone induction and prior to the introduction of the volatile agent under study. These were either within the normal range or only slightly elevated when measured following induction of anaesthesia, and it was always possible to obtain normocarbia within 2–4 minutes. We realised that there would be a decreasing level of narcosis at this time, but felt that awareness would be most unlikely to occur during such a short interval.

Dr Okell expressed particular concern that the children given isoflurane or enflurane may not have received adequate anaesthesia. His misgivings appear to be based on the assumption that a value of MAC awake 0.6 derived from adult volunteers recovering from halothane anaesthesia[1] is applicable to children and to isoflurane and enflurane. There is no evidence that this is the case and, indeed, the findings of Morris[2] suggest that in children an MAC awake 0.3 (approximate) may be more accurate for halothane; also, a recent study of the elimination of isoflurane in children by Wren *et al.*[3] would seem to indicate that MAC awake 0.2 (approximate) is a comparable figure for the newer agent. These data suggest that there is little likelihood of the children we studied being 'awake'. It should also be remembered that factors influencing MAC during the elimination of volatile anaesthetics may be quite different from those present during induction[4] and MAC values may well be higher during recovery.

It is our belief that wakefulness would be extremely unlikely after a thiopentone induction followed within a few minutes by 1% inspired halothane, enflurane or isoflurane, particularly when used with pancuronium which may further reduce the patient's requirements of these agents.[5] This opinion is based on our clinical experience of administering volatile anaesthetics to children and our impression that awareness is an uncommon feature of paediatric anaesthesia.

More importantly, none of the children we studied showed any clinical evidence of awareness or other manifestations of inadequate anaesthesia. We received no report of wakefulness or other adverse comments from the children nor from their parents or recovery room nursing staff.

The Royal Belfast G.W. BLACK
Hospital for Sick Children, T.M. GALLAGHER
Belfast BT12 6BE

References

1. Stoelting RK, Longnecker DE, Eger EI II. Minimum alveolar concentrations in man on awakening from methoxyflurane, halothane, ether and fluroxene anesthesia. *Anesthesiology* 1970; **33:** 5–9.
2. Morris P. Measurement of end-tidal halothane during recovery from anaesthesia. *Proceedings of the Association of Paediatric Anaesthetists of Great Britain and Ireland.* Abbott Laboratories, 1984.
3. Wren WS, McShane AJ, McCarthy JG, Lamont BJ, Casey WF, Hannon VM. Isoflurane in paediatric anaesthesia. Induction and recovery from anaesthesia. *Anaesthesia* 1985; **40:** 315–23.
4. Eger EI II. *Anesthetic uptake and action.* Baltimore: Williams and Wilkins Co., 1974.
5. Forbes AR, Cohen NH, Eger EI II. Pancuronium reduces halothane requirement in man. *Anesthesiology* 1979; **51:** S1.

Anaesthesia for extracorporeal shock wave lithotripsy

There are a few points which were not mentioned in the otherwise comprehensive coverage of the paper by Drs Abbott, Samuel, and Webb (*Anaesthesia* 1985; **40:** 1065–72).

The renal calculi are positioned in the focus of the shock wave reflector by using X ray and are supposed to remain within about 1 cm of this point for maximum energy transfer to the calculus. It has been necessary, in my experience, to reduce the usual tidal volume of 10 ml/kg/minute to 5 ml/kg/minute to reduce renal movement during intermittent positive pressure ventilation, and to increase the respiratory rate to maintain an acceptable end tidal carbon dioxide level. Patients who received spinal or epidural anaesthesia were sometimes unable to maintain a suitably small respiratory excursion to keep the calculus still.

Secondly, the authors recommend that a loss of resistance test with saline solution is used for epidural placement, to avoid the damage to nerves which might occur if the shock wave encountered an air–fluid interface such as that produced when air is used to locate the epidural space. This may not be as important as they claim. Firstly, the shock wave is focussed at the calculus, and so the energy density at sites in the path of the wave will be less than at the focus. Secondly, not all the energy is transferred to the calculus, and yet (as far as I am aware), there have been no reports of damage to air-containing viscera in the exit path of the wave. Finally, we have performed lithotripsy on one patient who had a horse-shoe kidney and had to be positioned prone, for two separate treatments. Both times he had no abdominal symptoms after his treatment, in spite of the wave traversing visceral air-fluid interfaces.

Finally, it is surprising that the patients in this study had a decrease in core temperature with a bath temperature of 36°C, since the thermoneutral temperature for humans immersed in water is reported to be 35–35.5°C.[1] In my experience, long treatments were associated with a drop in core temperature, but this was associated with a decreased water temperature and could be eliminated by starting with the water at 37–38°C.

Wycombe General Hospital, J.D. Young
High Wycombe,
Bucks. HP11 2TT

Reference

1. Craig AB Jr, Dvorak M. Thermal regulation during water immersion. *Journal of Applied Physiology* 1966; **21:** 1577–85.

A reply

Our paper was based on an investigatory study to determine methods of safe anaesthesia for extracorporeal shock wave lithotripsy. We were dependant on the advice given to one of the authors (DRW) during a visit to a working lithotripter in Mainz, Germany since no literature on the subject was published at that time. We may have to modify our recommendations in the light of the experiences of others with the passage of time.

We accept Dr Young's suggestion that a reduction in tidal volume reduces renal movement and thus improves the efficiency of the shockwaves, but conventional mechanical ventilation (CMV) is still not able to match high frequency jet ventilation (HFJV) in producing adequate pulmonary gaseous exchange with minimal renal movement (mean movement for CMV of 30.6 mm and for HFJV of 2.2 mm.[1] This leads to a reduction in the number of shock waves per given treatment, a lowering of the kilovoltage intensity, a shorter treatment time and an increase in electrode life.[2] The not insubstantial financial savings will soon repay the capital cost of the jet vetilator.

Dr Young claims to be unaware of any reports of damage due to exit path shock waves. If he would care to read Chaussy's book,[3] he will learn that fatal haemoptysis has occurred in experimental animals. In our paper we commented on the need to ensure that the shock wave exit site is immersed, otherwise painful erythema will result. This injury occurred in one of our patients. In view of these observations, we still recommend a loss of resistance to saline technique in order to avoid any possibility of damage to nervous tissue.

The temperature range quoted as thermoneutral for humans was derived from experiments on awake volunteers. Our observations were made on anaesthetised, paralysed patients whose lungs were ventilated with dry anaesthetic gases at room temperature. The inability to generate even basal amounts of heat combined with the cooling effect of mechanical ventilation may explain the small fall in core temperature seen in some of our patients. A higher initial water temperature than we used may be the solution.

Department of Anaesthetics,
Royal College of Surgeons,
Lincoln's Inn Fields,
London WC2A 3PN

M.A. ABBOTT
J.R. SAMUEL
D.R. WEBB

References

1. CARLSON CA, BOYSEN PG, BANNER MJ, GRAVENSTEIN JS. Conventional vs high frequency jet ventilation for extracorporeal shock-wave lithotripsy. *Anesthesiology* 1985; **63:** A530.
2. SCHULTE AM, ESCH J, KOCHS E, MEYER WH. Improved efficiency of extracorporeal shock wave lithotripsy during high frequency jet ventilation. *Anesthesiology* 1985; **63:** A177.
3. CHAUSSY C. (ed.). *Extracorporeal shock wave lithotripsy.* Basel: S. Karger, 1982; 34–5.

Carbon dioxide elimination during apnoea

We wish to illustrate a gross example of a commonly seen phenomenon. In a paralysed patient in whom ventilation is temporarily halted, the reservoir bag is often seen to oscillate in time with the pulse. Obviously little gas exchange occurs in these circumstances. This slight movement of gas has been used in conjunction with pneumotachography to give a crude measure of left ventricular function.[1] The figure shows the ECG and end tidal CO_2 trace of a febrile 11-year-old child who weighed 48 kg, undergoing appendicectomy. He had received thiopentone 250 mg, suxamethonium 60 mg, alcuronium 10 mg and fentanyl 100 μgm. His lungs were ventilated with nitrous oxide, oxygen and enflurane 1% via a Bain system with a Penlon Nuffield ventilator. Frequency of ventilation was 15/minute, with a tidal volume of 500 ml and fresh gas flow of 6 litres/minute. At the time of this recording, the pulse was 110/minute, arterial blood pressure 100/70 mmHg and the end tidal CO_2 was 37 mmHg.

The sampling point for the capnograph was at the catheter mount: in the figure, end tidal CO_2 values increase from top to bottom. Instead of the usual plateau during expiration, there is a sawtooth appearance in time with the pulse. In some instances, this is almost sufficient to shift the end tidal CO_2 values from inspiratory to expiratory levels within one cardiac cycle. This implies a degree of useful gas exchange. The authors have not encountered such a pronounced passive movement of respiratory gases before.

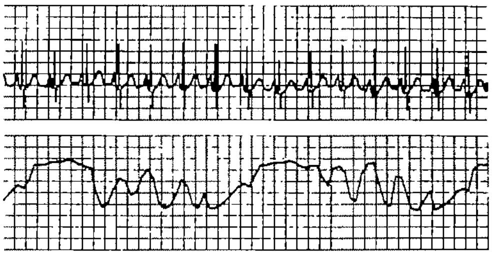


Fig. 1

Department of Anaesthesia,
Southampton General Hospital,
Southampton,
Hants. SO9 4XY

J.F. STUBBING
J.R.D. LAYCOCK

Reference

1. REITAN JA, LIM A. Automated measurement and frequency analysis of the pneumocardiogram. *Anesthesia and Analgesia* 1978; **57:** 647–52.

Acupressure and postoperative vomiting

Your editorial (*Anaesthesia* 1986; **41:** 1–3) painted a gloomy picture of current therapy of postanaesthetic nausea and vomiting. Your readers may perhaps be interested in the following trial.

Five hundred consecutive patients anaesthetised by the author were placed randomly in two groups using the hospital registration number. Patients in the treatment group had acupressure applied to the front of the wrist for thirty seconds just before induction of general anaesthesia and for another thirty seconds before leaving the operating theatre.

The patient's wrist is held so that even pressure is applied by the flexor surfaces of the index, middle and ring fingers to the distal 5 cm of the flexor surface of the forearm. This is approximately over the pronator quadratus muscle or alternatively the tendons of the superficial flexor muscles of the forearm. The force exerted should be sufficient to transmit the pressure to the deep structures, but not so great that discomfort is caused to a conscious patient or damage done to an unconscious one, perhaps the force should be similar to that of a firm hand shake.

One finger was placed over the skin creases of the front of the wrist with two more just proximal. The thumb supplied counter pressure. Patients in the control group were given similar anaesthetics for the category of operation, but the acupressure was not performed. It was not possible to use one anaesthetic technique for all the operations performed, but care was taken to give the same agents to all the cases within each category.

The patients did not know that they were in a trial. They were not told why their wrists were being squeezed. The trained nursing staff, who assessed the patients in the recovery ward, neither knew into which group the patients had been placed nor the purpose of the trial. The patients were asked four questions about pain, cold, sickness and thirst, to divert their attention, and that of the staff, from nausea and vomiting just before they left for the surgical ward; the answers were recorded.

There were 131 men and 119 women in the control group, with a mean age of 39.9 years and a mean operating time of 43.7 minutes. In the acupressure group there were 136 men and 114 women, with a mean age of 41.1 years, and a mean operating time of 41.7 minutes. The patients were evenly spaced over the following categories of operation: ophthalmic surgery 43:37 (4:2), ear nose and throat surgery 42:45 (4:1), orthopaedic surgery 29:30 (6:0), general surgery (major) 60:63 (11:5), general surgery (minor) 76:75 (15:3). The figures in brackets refer to the number of patients in that particular category who were, or who complained of feeling, sick (control: acupressure groups). Eleven patients in the acupressure group and forty patients in the control group felt or were seen to be sick, $\chi^2 = 18.36$, $p = <0.001$.

This very simple manoeuvre is thus shown to be associated with a significant reduction in the incidence of nausea and vomiting during the immediate recovery period following general anaesthesia given for a variety of operative procedures. Its action is brief, 5–30 minutes, so if the stimulus to nausea continues nausea and vomiting will recur. It does not replace the anti-emetic action of antihistamine or phenothiazine drugs but it will be effective in the prevention or treatment of self-limiting conditions such as nausea and vomiting following general anaesthesia. Due to its quick onset of action, it may suppress vomiting even after retching has begun, as long as gastric contents have not reached the pharynx; this enables it to be used to reduce nausea and vomiting before anti-emetic drugs can act and to postpone threatened vomiting while patients are being transported on trolleys or during various invasive procedures when it would be inconvenient or dangerous to move them.

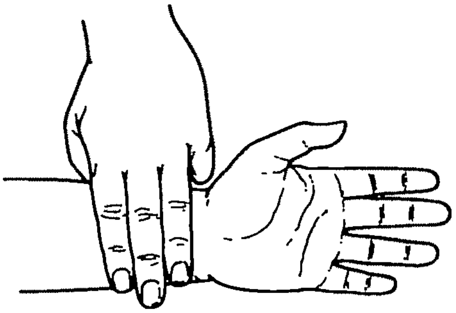


Fig. 1.

North Tees General Hospital,
Stockton on Tees,
Cleveland TS19 8PE

E.N.S. Fry

Aortic knuckle and tracheal obstruction

We consider that the reason given in the article by Drs Sapsford and Snowdon (*Anaesthesia*, 1985; **40:** 552–4), for obstruction of the tracheal tube by a prominent aortic knuckle is unlikely. The term aortic knuckle is the name given to the shadow cast by the terminal part of the arch of aorta seen in antero-posterior radiographs. The anatomical relations of the terminal part of the arch of the aorta (aortic knuckle) are such that it lies to the left as well as posterior to the trachea.[1] Hence the aortic knuckle (terminal part of the arch of the aorta) is not in direct relationship with the trachea and it appears unlikely to be the cause of obstruction to a tracheal tube. Even though the arch of the aorta is related posteriorly to the trachea, the elastic walls of the arch of the aorta would not press upon the trachea, which has rigid walls because of its hyaline cartilaginous rings and obstruction of the tracheal tube would not follow.

Department of Anaesthesiology
and Department of Anatomy,
S.R.T.R. Medical College,
Ambajogai, Dist. Beed,
Maharashtra, India 431517

G.S. Sarate
S.N. Sant

Reference

1. Warwick R, Williams PL. (eds). *Gray's anatomy*, 35th edn. Edinburgh: Longman Group Ltd, 1973, 619–21.

A reply

We would like to thank Drs Sarate and Sant for their interest and wish to make the following observations.

The term 'aortic knuckle' or 'aortic knob' is a specific feature of radiological anatomy and is that part of the aortic arch that is seen end on in a frontal chest radiograph.[1] It lies immediately to the left of the trachea, above the main pulmonary artery. Deviation of the lower part of the trachea is related to the aorta, becomes more marked with age, and is often pronounced when there is dilatation of the aorta.

We note the letter by Drs Martin and Hutchinson[2] also strongly supports the view that the trachea may indeed be deformed by the aorta and that this can cause obstruction of the tracheal tube.

Departments of Anaesthesia
and Radiodiagnosis,
Royal Liverpool Hospital,
P.O. Box 147,
Liverpool L69 3BX.

D.J. Sapsford
S.L. Snowdon
G.H. Whitehouse

References

1. GRAINGER RG, ALLISON DJ (eds). *Diagnostic radiology*. Fleischer Society; Glossary of 'chest' radiological terms. Edinburgh and London: Churchill Livingstone, 1985: 367.
2. MARTIN J, HUTCHINSON B. Tracheal tube obstruction by prominent aortic knuckle. *Anaesthesia* 1986; **41:** 86–7.

Anaesthesia in idiopathic autonomic dysfunction

The case report of Sweeney *et al.* (*Anaesthesia* 1985; **40:** 783–6) raises several questions. In cases of idiopathic autonomic dysfunction (IAD) with postural hypotension, there are several treatment regimens to reduce the severity of this life threatening complication; the mainstays are graded elastic stockings, postural training during sleep and 9-fludrocortisone. Pre-operative institution of these regimens may or may not reduce the incidence of peri-operative hypotension.[1,2]

In a patient who has received no maintenance therapy for postural hypotension, a severe decrease in blood pressure can be anticipated with cardiodepressant drugs, intermittent positive pressure ventilation (IPPV), posture and hypovolaemia. These problems will usually be readily reversed by infusion of fluid or lifting the legs. However, these patients have a relatively fixed cardiac output with no alteration in pulse rate in response to haemodynamic change. This will make the assessment of hypovolaemia more difficult and its consequences more serious. In view of this, central venous pressure (CVP) monitoring can be very helpful as a guide to the patient's blood volume status, allowing anticipation of and prevention of the sudden and profound arterial pressure falls reported by Sweeney and others.[1,3]

A further indication for some kind of monitor of cardiac filling pressures is illustrated by our case report of anaesthesia in a 65-year-old patient with Shy-Drager syndrome.[2] In this case, complicated by a myocardial infarction some 7 years prior to surgery, the patient was sensitive to fluid overload and cardiac failure was readily precipitated. In view of the possibility of impaired left ventricular (LV) function and hence unreliability of CVP measurements in this case, we chose to monitor pulmonary artery wedge pressure (PAWP) in addition to CVP. After stabilising blood volume prior to surgery, controlled ventilation of the lungs and muscle paralysis after etomidate; no decrease in arterial pressure was recorded. We had no problems with respiratory depression postoperatively and can shed no further light on the cause of respiratory depression.

Sweeney *et al.* also mention the patient's high threshold for painful stimuli and sensitivity to anaesthetic agents. While it is true to say that these patients may exhibit haemodynamic sensitivity in response to anaesthetic drugs, it is difficult to comment upon their pain threshold. Autonomic dysfunction precludes any sympathetic response to pain; hence, the fact that their patient at no times showed a pressor response or signs of increased sympathetic tone in response to stimulation does not necessarily indicate lack of perception of pain.

In conclusion, in the management of a patient with IAD undergoing surgery, particularly where blood loss may be anticipated, it would seem preferable in an elective case to attempt to control the patient's postural hypotension pre-operatively. The anaesthetic technique should then attempt to avoid major decreases of blood pressure by the use of induction agents without gross cardiac effects, careful positioning on the operating table and the avoidance of hypovolaemia. Direct monitoring of fluid losses, central venous pressure, arterial pressure, urine output and peripheral perfusion allows anticipation and prevention of severe hypotension. Monitoring of PAWP may be useful in patients with poor LV function. In view of the respiratory depression seen in this case report and lack of arterial pressure falls with IPPV seen in our report, a technique involving IPPV may be appropriate.

Royal Children's Hospital, R.C. HUTCHINSON
Melbourne,
Victoria, 3052,
Australia

References

1. COHEN CA. Anesthetic management of a patient with Shy-Drager syndrome. *Anesthesiology* 1971; **35:** 95–7.
2. HUTCHINSON RC, SUGDEN JC. Anaesthesia for Shy-Drager syndrome. *Anaesthesia* 1984; **39:** 1229–31.
3. BEVAN DR. Shy-Drager syndrome. A review and a description of the anaesthetic management. *Anaesthesia* 1979; **34:** 866–73.

A reply

Optimal pre-operative treatment of patients with idiopathic autonomic dysfunction (IAD) should be carried out whenever possible. Nevertheless, as our case illustrates, patients will continue to present for anaesthesia who are either undiagnosed or who, for whatever reason, have not received the appropriate treatment. In an emergency, the risks associated with anaesthesia in these patients may have to be accepted.

We agree that central venous pressure (CVP) monitoring in these patients does provide some help in the assessment of the patient's blood volume status. However, isolated readings of CVP may be misleading and trends or the response to repeated fluid challenges may be of more value. We feel, however, that the measurement of left atrial pressure (LAP) using a pulmonary arterial catheter must be questioned. There is no doubt that LAP measurement is helpful in certain cases, such as the one cited,[1] of a patient with impairment of left ventricular function following a myocardial infarction. The benefit to the patient under these circumstances will obviously outweigh the risks. However, in the otherwise healthy patient, routine insertion of a pulmonary artery catheter may be unhelpful.

It is true to say that autonomic dysfunction precludes any sympathetic response to pain and it may therefore be true that sensitivity to pain may merely be undetected by the conventional observation. Nevertheless, alteration in pain threshold is a well recognised feature of certain other autonomic neuropathies, for example the Riley Day syndrome, and it has been postulated that these patients may be depleted in substance P.[2] The anaesthetic implications of this for any particular patient are, of course, crucial and it would seem that the only solution to this dilemma would be to test the patient's sensitivity to pain pre-operatively.

Department of Anaesthesia,
St Bartholomew's Hospital,
London EC1A 7BE

B. SWEENEY
S. JONES
R.M. LANGFORD

References

1. HUTCHINSON RC, SUGDEN JC. Anaesthesia for Shy-Drager syndrome. *Anaesthesia* 1984; **39:** 1229–31.
2. PEARSON J, BRANDEIS L, CUELLO AC. Depletion of substance P—containing axons in substantia gelatinosa of patients with diminished pain sensitivity. *Nature* 1982; **295:** 61–3.

Difficult intubation

In the light of recent reports on difficult laryngoscopy,[1,2] the following case is interesting.

A woman aged 57 years who weighed 65.5 kg, was scheduled for diagnostic laparoscopy. It was known that she had had previous operations including ovarian cystectomy and cholecystectomy and there was no record of any problems with anaesthesia. Induction was with thiopentone 350 mg followed by atracurium 25 mg. It proved impossible, after waiting for full relaxation, to expose even the tip of the epiglottis, let alone the larynx, with an adult blade Macintosh laryngoscope. This accords with class 3 difficulty.[3] The patient's head was repositioned on a higher pillow, a long-bladed laryngoscope was used and a malleable introducer was tried. In between attempts the patient was kept well oxygenated and ventilated with nitrous oxide, oxygen and halothane. Relaxation seemed adequate, but an additional 15 mg atracurium was given and, eventually, with the aid of a gum elastic bougie, a tracheal tube was passed blind. The epiglottis was never seen.

Postoperative X rays of the cervical spine (Figs 1 and 2) revealed a very small atlanto-occipital space

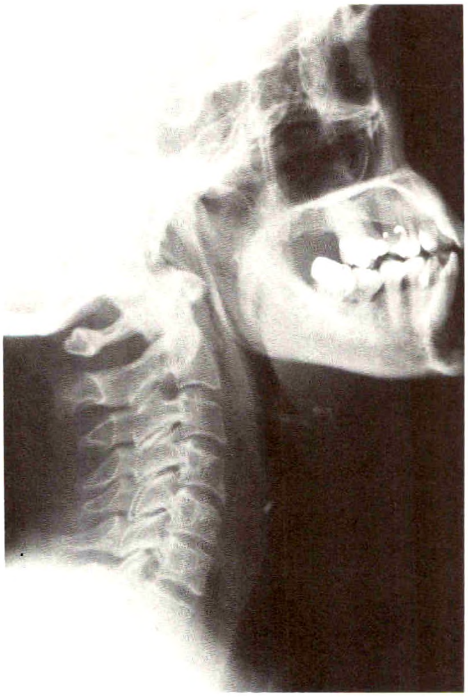


Fig. 1.

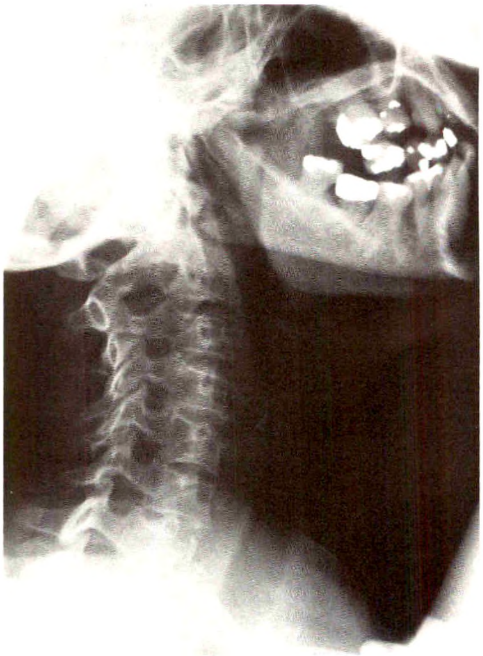


Fig. 2.

(1 mm), a deep mandibular ramus (3.5 cm) and protruding upper incisors: the combination that suggests that difficulty might have been expected.[2] Application of Cormack's formula.[2]

$$Y = 27.1 - 12.2x_1 + 1.3x_2$$

gives a value for Y of -14.3. Any negative value for Y indicates difficulty, and in this case it is very negative!

In Fig. 1 it can be seen that there is a degree of anterior bowing of the cervical spine even in the neutral position; Fig. 2 shows the increased bowing that occurs when head extension is attempted, carrying the larynx forward, as described by Nichol and Zuck.[4]

Farnborough Hospital,
Orpington,
Kent

A.S. Nathan
J.G. Scott
M. Mohandas

References

1. Levack ID, Masson AHB. Difficult tracheal intubation in obstetrics. *Anaesthesia* 1985; **40:** 384.
2. Zuck D. Difficult tracheal intubation. *Anaesthesia* 1985; **40:** 1016–7.
3. Cormack RS, Lehane J. Difficult tracheal intubation in obstetrics. *Anaesthesia* 1984; **39:** 1105–11.
4. Nichol HC, Zuck D. Difficult laryngoscopy—the anterior larynx and the atlanto-occipital gap. *British Journal of Anaesthesia* 1983; **55:** 141–4.

Intermittent mandatory ventilation for children

Intermittent mandatory ventilation (IMV) is commonly required to wean children from controlled ventilation after cardiac surgery. We have found that using the Siemen's Elema 900B or 900C ventilators, the initial step to f/2 in the IMV mode is often not tolerated by the patient and a more gradual reduction in frequency is necessary.

The change of ventilator settings in order to wean the patient gradually and to impose the same tidal volume and inspiratory time is a matter of simple arithmetic, but can be tiresome. Furthermore, to retrace one's steps and to attempt to reproduce intermediate points in the preceding weaning process from current variables can result in inappropriate ventilator settings.

The following scheme allows values and settings to be substituted, which allow close approximation to the desired tidal volume and inspiratory time. A computer program has been written which will produce an individual print-out of the initial Servo settings and IMV parameters necessary to decrement support in 5 breath steps. A copy of the original program can be obtained from the first author.

Killingbeck Hospital,
York Road,
Leeds LS14 6UQ

A.D. Crew
I.C. Grant
M. Ward

Table 1. Example print-out

Rate (RR)	Minute volume (MV) litres	Tidal volume (TV) ml	Inspiratory time (IT) (insp % + pause %) × 60/(RR × 100) seconds	End expiratory pressure (PEEP) kPa
30	3.0 litres	100 ml	(25% + 10%) 0.7	+ 0.5

Desired rate (DR)	Set F	Set Rate (SR) DR × F	Set minute volume SR × TV (L)	Total insp % IT × SR × 100/60	Set insp %	Set pause	Set PEEP kPa
25	F/2	50	5.0	58%	33	20	0.5
20	F/2	40	4.0	47%	33	15	0.5
15	F/2	30	3.0	35%	25	10	0.5
10	F/2	20	2.0	23%	20	5	0.5
6	F/5	30	3.0	35%	25	10	0.5

Continuous infusion with vascular monitoring

The report of the problem encountered by Drs Ryan and Wise (*Anaesthesia*, 1985; **40:** 1134–5), when parenteral feed was found to be backing up through the central venous pressure (CVP) transducer and in danger of being infused arterially was interesting. We are all party to a variety of complicated plumbing exercises from time to time in our patients in intensive care units, and it may be that this problem occurs more often than we realise; one result might be of inappropriate response to certain drugs due to the infusion travelling along the wrong tube in the wrong direction.

Might I recommend one possible solution to the problem, namely that we should use one of the commercial multiple lumen catheters. These are inserted in the usual way over a guide wire, with no more difficulty than most other venous catheters. One lumen can then be used exclusively for continuous online CVP monitoring and the others for fluid infusions, parenteral nutrition, or drug infusions. Some plumbing may still be required, but similar infusion devices can be grouped together as appropriate through a lumen separate to that used for the CVP monitoring.

Department of Anaesthesia,
Manchester Royal Infirmary,
Oxford Road,
Manchester M13 9WL

B.J. POLLARD

Vecuronium in the myasthenic patient

We were interested to read the article on this subject by Hunter *et al.* (*Anaesthesia* 1985; **40:** 848) because we have recently used vecuronium in five myasthenic patients undergoing *transcervical* thymectomy (the operation presumably undergone by their six patients). We would like to make several comments on their report.

Hunter states that muscle relaxants 'are usually required only in upper abdominal and thoracic procedures', and that all patients were intubated 'without difficulty', 90 seconds after administration of vecuronium 0.02 or 0.04 mg/kg intravenously. However, in a previous report by one of Hunter's group,[1] 22 myasthenic patients successfully underwent transcervical thymectomy without use of either muscle relaxants or potent inhalational agents; anaesthesia was achieved with Althesin or etomidate, and fentanyl, and all patients were intubated within 3 minutes of the completion of induction. The muscle relaxation requirement for this surgical procedure would therefore seem to be controversial. In our experience, relaxation considerably facilitates both tracheal intubation and surgical access for this procedure.

In regard to vecuronium dosage, whereas Hunter found that two-fifths of the normal (intubating) dose (0.04 mg/kg) produced a T1/control ratio of 20%, in our patients we found that this effect was produced by only 0.011 mg/kg (range 0.003–0.020). Furthermore, the mean total dose of vecuronium in our patients was 0.03 mg/kg as compared to the 0.104 mg/kg which we have calculated from the data reported by Hunter *et al.* in their Table 2.

The difference in sensitivities may not be quite so great, however, since we believe that there are errors in Hunter's Table 2. This reports 'incremental dosage (μ/kg) as 0.4 and 0.8, yet the summary and text report 4 μg/kg (patients 1 and 2), and double this (8 μg/kg in patients 3–6). The 'total doses of vecuronium (mg/kg)' in Table 2 would also seem to be in error. Thus, according to the text, patient 2 received an initial dose of 0.02 mg/kg, followed by 9 doses of 4 μg/kg, giving a total dose of 0.056 mg/kg, rather than the 0.1 mg/kg stated in the table. Similar errors exist in patients 3–6 in Table 2; only patient 1 is reported correctly. We have recalculated the total dosages for Hunter's patients based upon the text and the number of incremental doses given. The results are shown in our Table 1. The mean total dose of vecuronium in Hunter's patients was 0.076 mg/kg.

Like their patients, ours were also clinical class I–IIB by the Osserman and Genkins classification,[2] pyridostigmine had been withheld on the morning of surgery and no potent inhaled agents were used. Are myasthenic patients in New York more sensitive to non-depolarising muscle relaxants than those in the UK? A transatlantic difference in curare sensitivities has been described among normal patients.[3] A species difference cannot be totally ruled out! None of our patients, however, was receiving therapy with azathioprine or prednisolone. In the series of five patients who received atracurium,[4] only one was reported as receiving these immunosuppressant drugs. It is therefore quite likely that the relative resistance to vecuronium suggested in Hunter's patients was related to their existing drug therapy. This might be worthy of further study, both in myasthenic and in normal patients.

One of the features offered by the intermediate acting non-depolarising relaxants, vecuronium and atracurium, is that reversal may not always be necessary. This is particularly advantageous in myasthenics, where

Table 1. Racalculation of total dose of vecuronium for Hunter *et al*'s patients (Hunter, Table 2)

Patient	Initial dose (μg/kg)	Incremental dose (μg/kg)	Number given	Total of increments (μg)	Total dose (mg/kg)
1	20	4	20	80	0.100
2	20	4	9	36	0.056
3	40	8	7	56	0.096
4	40	8	6	48	0.088
5	40	8	2	16	0.056
6	40	8	3	24	0.064
				Mean	0.076

an overdose of anticholinesterase may increase weakness by producing a cholinergic crisis.[5] In this respect, we believe that the use of two doses of neostigmine 2.5 mg, given intravenously 5 minutes apart, may cause problems. Thus, 1 mg intravenous neostigmine, 4 mg intravenous and 120 mg oral pyridostigmine are equivalent dosages of anticholinesterase.[6] The neostigmine 5 mg which was given intravenously is therefore equivalent to pyridostigmine 600 mg orally, yet the average total *daily* dosage of pyridostigmine in Hunter's patients was only 327.3 mg!

Titration of anticholinesterase would seem to be more appropriate and Foldes has recommended pyridostigmine intravenously in 1 mg increments.[6] Admittedly, Hunter *et al.* gave 2.5 mg neostigmine intravenously, followed 5 minutes later by a further 2.5 mg. However, Miller *et al.*[7] have shown that the mean time from administration of intravenous neostigmine 1.8 mg/sq m to peak antagonism of relaxation was 7.1 minutes. Thus, adequate time did not elapse to assess the maximum effect of neostigmine. Reference to Fig. 3 in Hunter's paper indicates that the second dose of neostigmine 2.5 mg did not further increase twitch or fade ratios and potentially may have precipitated a cholinergic crisis. Edrophonium now might well be the agent of choice for reversing residual curarisation, because its time from onset to peak effect is the least of all of the anticholinesterases, making careful titration of dose against effect that much easier.

We agree with Hunter *et al.*, that even when the disease is to some degree under control with therapy, myasthenic patients appear to remain sensitive to the effects of the competitive relaxants. Indeed, one of us (JBE) has observed an increased sensitivity to atracurium in a myasthenic patient in true remission; this patient was asymptomatic and off all therapy for 3 years at the time the relaxant was administered.

In conclusion, many different approaches to the anaesthetic management of the myasthenic patient have been advocated and all have their place. In our experience, provided that there is careful titration of dose against mechanomyographic (twitch) or integrated electromyographic monitoring of response, all competitive neuromuscular blockers can be safely used in patients with myasthenia gravis.

Department of Anesthesiology,
The Mount Sinai Medical Center,
New York,
NY 10029, USA

J.B. Eisenkraft
R.K. Sawhney
A.E. Papatestas

References

1. Florence AM. Anaesthesia for transcervical thymectomy in myasthenia gravis. *Annals of the Royal College of Surgeons of England* 1984; **66:** 309–12.
2. Osserman KE, Genkins G. Studies in myasthenia gravis: review of a twenty-year experience in over 1200 patients. *Mount Sinai Journal of Medicine* 1971; **38:** 497–537.
3. Katz RL, Norman J, Seed RF, Conrad L. A comparison of the effects of suxamethonium and tubocurarine in patients in London and New York. *British Journal of Anaesthesia* 1969; **41:** 1041–7.
4. Bell CF, Florence AM, Hunter JM, Jones RS, Utting JE. Atracurium in the myasthenic patient. *Anaesthesia* 1984; **39:** 961–8.
5. Havard CWH, Scadding GK. Myasthenia gravis. Pathogenesis and current concepts in management. *Drugs* 1983; **26:** 174–84.
6. Foldes FF, Nagashima H. Myasthenia gravis and anesthesia. In: *Endocrinology and the anesthetist*. Elsevier Science Publishers B.V., 1983.
7. Miller RD, Van Nyhuis LS, Eger EI II, Vitez TS, Way WL. Comparative times to peak effect and durations of actions of neostigmine and pyridostigmine. *Anesthesiology* 1974; **41:** 27–33.

A reply

We are grateful to Drs Eisenkraft, Sawhney and Papatestas for pointing out the arithmetical errors in Table 2 of our paper; the revised figures given in Table 1 of their letter are indeed correct, as indeed are those in our summary.

We did not suggest in our paper that a muscle relaxant was essential for cervical thymectomy. This group of myasthenic patients was only a suitable pool for study. In about 30% of the myasthenic patients in this centre having thymectomy, however, the cervical incision is extended to a sternotomy; use of a muscle relaxant drug may well then be an advantage.

We have always felt that there is a wide spectrum of disease in myasthenia gravis and in any study where the number of patients is small, which is almost inevitable in such an uncommon disease, there will be a definite variation between patients. This variation will also be manifest when the results from different studies are combined and surely this factor, rather than a transatlantic difference, is the cause of the slight variation in dose requirements of muscle relaxants between the two studies. Neostigmine 2.5 mg would no doubt have produced sufficient reversal of residual neuromuscular blockade in our study, but we saw no evidence whatsoever of the suggested cholinergic effects from neostigmine 5 mg.

We feel that the important point in the use of both atracurium and vecuronium in myasthenia gravis is that very manageable, albeit reduced, doses of these two newer agents can be used much more effectively than the more conventional relaxants if neuromuscular monitoring is employed throughout anaesthesia.

University Department
of Anaesthesia,
Royal Liverpool Hospital,
PO Box 147
Liverpool L69 3BX

Jennifer M. Hunter

Malignant hyperpyrexia susceptibility and childbirth

This is an account of the anaesthetic management, during the perinatal period, of a patient susceptible to malignant hyperpyrexia (MH). This had been diagnosed on muscle biopsy following a reaction during anaesthesia when she was 7 years old. She was booked for delivery in this unit in her first pregnancy aged 17 years.

Normal pregnancy and labour have not been reported to trigger MH and it was therefore planned to manage labour under epidural analgesia, which could be extended for instrumental or operative delivery if necessary. If general anaesthesia were needed, a safe technique using thiopentone, nitrous oxide, oxygen fentanyl and vecuronium was planned, administered via a vapour-free system and an automatic ventilator. Vecuronium was chosen because it has a rapid onset and short duration of action, which would facilitate rapid intubation and avoid the need for atropine and neostigmine at the end of surgery.

She presented with a history of contractions at 38 weeks of gestation. Her cervix was dilated 1 cm and the membranes were intact. She was not initially thought to be in established labour and was given intramuscular pethidine 75 mg for pain relief. Ninety minutes later the contractions were regular and the cervix was dilated to 2 cm. Epidural analgesia was established using 0.5% plain bupivacaine.

The pulse, arterial pressure and axillary temperature were measured hourly. The patient was not anaesthetised, so more invasive monitoring was not considered necessary because symptoms of respiratory distress would indicate the onset of MH to the writer, who was present throughout. Dantrolene, although readily available, was not given prophylactically.

Labour progressed uneventfully, except for a steady rise in temperature to 38.6°C approximately 5 hours after the epidural was established, when fetal distress was diagnosed and she had a forceps delivery of a 3.96 kg infant (Apgar score 9 at 1 minute). Throughout labour and delivery she remained pain-free and on direct questioning had no symptoms attributable to a high level of metabolic activity. Her pulse remained between 85 and 100 beats/minute and her arterial blood pressure was stable between 130/70 and 100/60 mmHg.

No cause for the pyrexia was found on clinical examination but blood cultures were taken and, although subsequently no organisms were isolated, intravenous ampicillin was started. Arterial blood gas analysis showed no hypoxia or metabolic acidosis. The results (on air) were pH 7.395, $P\text{aco}_2$ 4.3 kPa, $P\text{ao}_2$ 13.4 kPa, base excess −5.2 and standard bicarbonate 19.6 mMol/litre. These values were not compatible with the diagnosis of MH and she was observed in the labour suite for a further 8 hours. Her temperature fell steadily to normal by the 5th day postnatally and she suffered no symptoms except transient dysuria on day 3, but repeated urine culture produced no growth.

The successful outcome of this case illustrates the importance of prior knowledge of the diagnosis so that appropriate precautions may be taken. A protocol for the management of this rare condition has now been established in this unit. The relevance of simple clinical monitoring is emphasised in the management of this patient. This was considered safe as signs of an impending attack of MH would not have been masked by general anaesthesia.

Liverpool Maternity Hospital,
Liverpool L7 7BN

D.J.A. Rose

Unusual cause of obstructed airway in a child

A 7-year-old girl with mild cerebral palsy presented for elongation of her Achilles tendon. Following an intravenous induction of anaesthesia with thiopentone it was obvious that her airway was difficult to maintain, and so, a size 2 Guedel style single use airway manufactured by Portex Ltd, was inserted; total respiratory obstruction resulted. This was partially relieved when the artificial airway was removed. The anaesthetic was deepened and after a few minutes the airway was reinserted, resulting once again in total obstruction. Removal again resulted in a partial return of breath sounds. The artificial airway appeared to be normal, but it was decided to insert a second one and this resulted in complete relief of the obstruction.

The first airway was re-examined more closely and Fig. 1 shows the cause of the obstruction. A fine plastic film was tightly stretched, investing its end, so as to be all but invisible without very close inspection. The origin of this film became obvious when the nurse, who opened the plastic bag which contained the airway, demonstrated her technique. As can be seen in Fig. 2 she used the sharp end of the airway to break it open with the result that the plastic stretched until it became very fine, rather like the film used for wrapping food.

This is a rare complication of using oropharyngeal airways, but the author has noted others using a similar

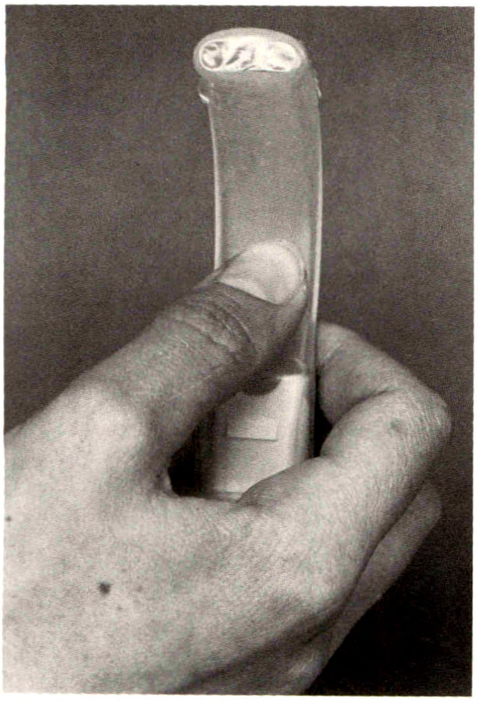


Fig. 1.

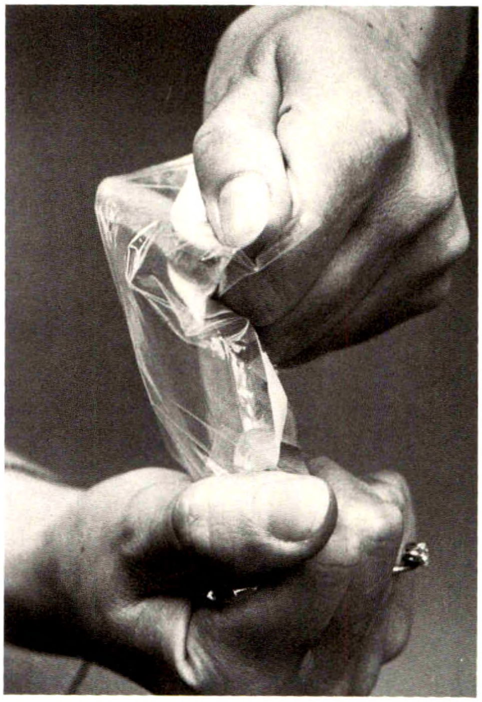


Fig. 2.

technique to open the plastic pouches and so there is a danger that it may be repeated. The recommended method of opening Portex oropharyngeal airways in plastic pouches is to use scissors.

Royal Hospital for Sick Children,
Yorkhill,
Glasgow G3 8SJ

L.R. McNicol

Transdermal glyceryl trinitrate

The recent article on the use of transdermal hyoscine (*Anaesthesia* 1986; **41:** 16–20) was interesting. This is a report of our use of transdermal glyceryl trinitrate as a mild vasodilator in elderly patients.

The first time it was suggested for use was in a rather frail, elderly female patient who was being assessed some 12 hours after an emergency laparotomy. She was considered to have received an adequate fluid replacement and had a stable pulse and arterial blood pressure since her operation, but intense peripheral vasoconstriction was still evident, with coldness of both legs which extended to mid-thigh level. Fluid challenge or traditional intravenous vasodilation both seemed something of a threat to this frail patient, and it was considered that perhaps transdermal glyceryl trinitrate should be tried, with the thought that it might also offer a beneficial cardiac effect at the same time. Both legs became pink and warm to the tips of the toes within three quarters of an hour.

Another impressive anecdote was that of an octogenarian who had undergone elective repair of a very large abdominal aortic aneurysm. The morning after his operation he was being treated with a renal-dose dopamine infusion to maintain urine function and although his general state was considered reasonable, there was some concern about the poor perfusion of the ankles and feet. Both feet rapidly became pink and warm after transdermal glyceryl trinitrate was started. Over the next few days he made steady progress until the third postoperative day when the feet were again cold and clammy. He was still on a very small dose of dopamine and neither clinical assessment nor the fluid balance chart gave any indication as to why the change had occurred. After a couple of hours of niggling frustration the glyceryl trinitrate skin patch was examined. It transpired that the nurse who changed the patch about 4 hours beforehand had omitted to remove the protective backing on the patch so that no drug was being administered. Hasty correction of this embarrassing situation restored the toes to a satisfying state of reassuring warm pinkness.

In the 18 months we have been using transdermal glyceryl trinitrate as a mild vasodilator in the elderly, we have seen no side effects. We use the 'Transiderm-Nitro

5' singly and change the patches every 24 to 36 hours. Our experience, though admittedly entirely anecdotal, is that this agent used in the way described deserves consideration for more widespread use.

Clatterbridge Hospital,
Clatterbridge Road,
Bebington,
Merseyside L63 4JY

P. CHARTERS

Overdose of intrathecal morphine

This is a report of about four patients who had orthopaedic operations under spinal anaesthesia ($L_{1/2}$ with 5% lignocaine and 0.15 *grams* morphine. The first patient was a 90-year-old lady with a femoral fracture. She also suffered from Parkinson's disease and chronic heart failure. The second patient was an 82-year-old lady with a femoral fracture, hypertension and chronic heart failure. The third patient was a 61-year-old man with a fractured patella, hypertension and previous history of cerebrovascular accidents. The fourth patient was a 78-year-old man with a femoral fracture and hypertension.

One and a half hours after surgery they developed drowsiness, apnoea, central cyanosis without cardiovascular effects. Tracheal intubation was performed and automatic ventilation of the lungs instituted. Nalorphine was administered and automatic ventilation was withdrawn 24 hours later without respiratory, cardiovascular or neurological complications.

Intrathecal morphine (2 mg) is used as a postoperative analgesic drug and in these cases 15 mg was given instead of 1.5 mg. This was due to an error in the dilution. No permanent harm occurred to the patients who were without pain for 4 days postoperatively; this helped in their mobilisation and their early discharge from hospital.

46 AG Fanouriou,
116 33 Athens,
Greece

S.P. POMONIS

Distress caused by urethral catheters

For many years the pain and distress caused to patients by indwelling urethral catheters has been either ignored or inappropriately treated.

Commonly, the degree of postoperative analgesia required to obtund surgical pain is sufficient to relieve the discomfort of an indwelling catheter. However, some patients requiring catheters have no surgical pain, and in others the catheter is often a more potent source of pain and suffering than the surgery itself. In the past, this pain may have been ignored completely as unimportant or treated by systemic analgesia of one sort or another; neither of these solutions is appropriate.

For the last year or so, I have been using a simple remedy with a high degree of success and patient gratitude; 30 ml of 0.25% plain bupivacaine is instilled up the catheter (ideally with the patient in a sitting or semi-recumbent position) and the catheter clamped for about 20 minutes. This allows the local anaesthetic to settle in the area of the sensitive trigone under the catheter balloon and produces rapid, prolonged pain relief. There may be some instances where bladder irrigation must be continued at all times and in these cases the method may be inappropriate. The risk of systemic absorption of the drug must be minimal (unless there are open venous sinuses) and the avoidance of unnecessary systemic analgesics is a real advantage. Early mobility can be accomplished in comfort.

Interestingly, repeat doses have rarely been necessary over a 24–48 hour period, since a single dose seemingly offers prolonged relief. This technique has not to my knowledge been reported before and I should be interested to read other views. It has seemed to me safe, simple and rewarding.

Department of Anaesthetics,
Plymouth General Hospital,
Plymouth,
Devon

M.B. COATES

An airtight seal between facemask and beard

There is an alternative method to achieve the same result as that suggested by Drs Lawes and Murrell (*Anaesthesia* 1985; **40:** 1142) in which your readers may be interested.

Water soluble gel is squeezed from a tube onto the patients' beard in a V-shape after induction of anaesthesia. The apex of the V should be on the chin and each limb of the V should extend towards an angle of the mouth, thus covering the beard where the rim of the facemask will be applied. Next, the gel is covered by two

WE'VE GIVEN YOU PRECISELY WHAT YOU WANTED

MORE DILUTE HYPNOVEL

When we asked how Hypnovel could be improved, many users asked for a more dilute presentation, so that finer control of dosage, and therefore sedation, could be achieved. So the 2ml presentation was joined by an ampoule containing the same 10mg of midazolam, but in 5ml of solution. The extra 3ml of diluent makes it simpler to obtain the full benefits of Hypnovel. Proven benefits of Hypnovel include fast onset and rate of recovery, excellent amnesia and minimal venous complications.[1]

THE HYPNOVEL 10mg/5ml AMPOULE

midazolam

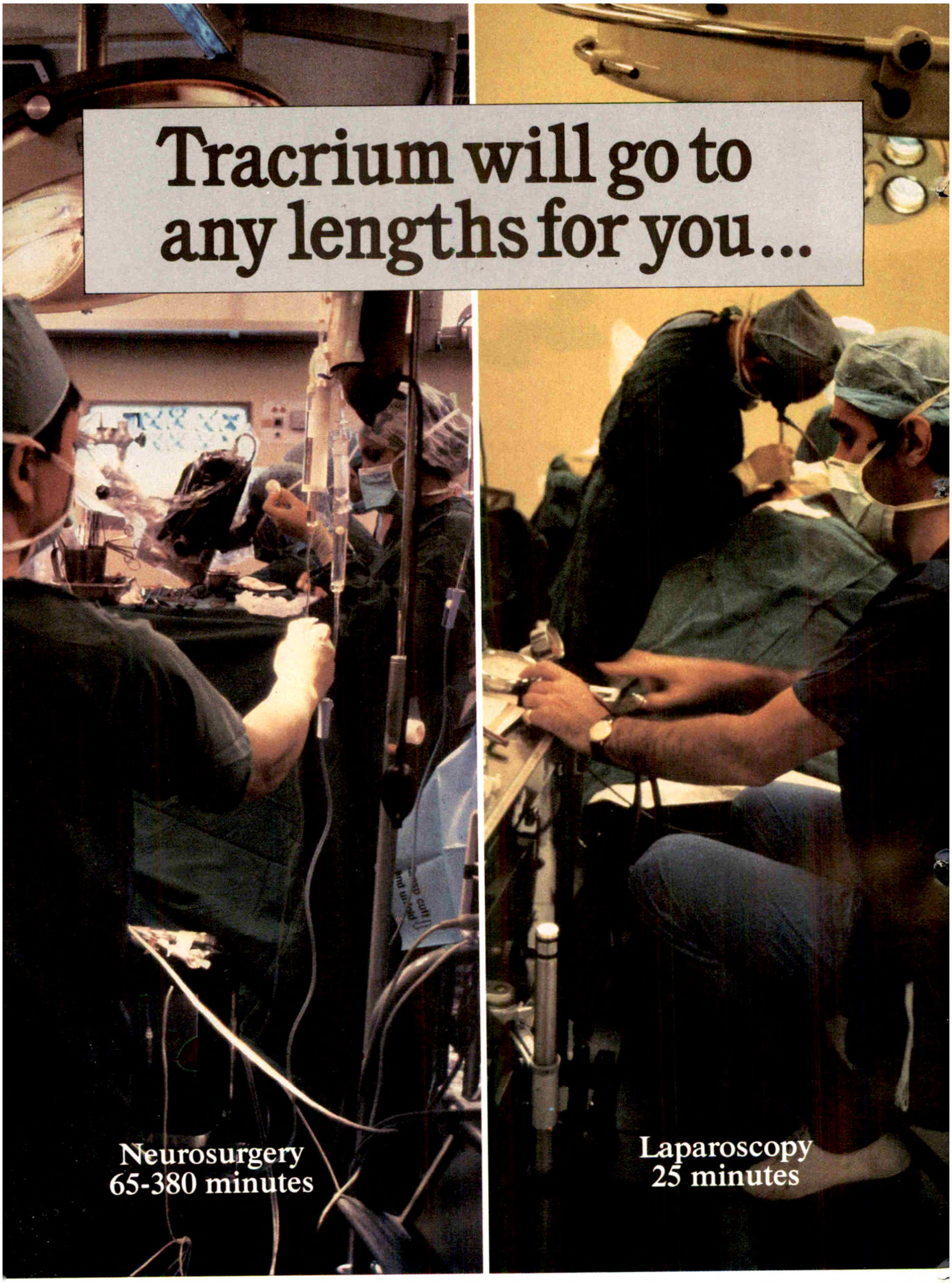
FOR MORE PRECISE CONTROL OF I.V. SEDATION

Prescribing Information

Indications Intravenous sedative cover. Alternative intravenous agent for induction of anaesthesia in high-risk patients. Intramuscular premedication. **Dosage and Administration** *Intravenous sedation* Usual total dose 2.5mg to 7.5mg (approx. 0.07mg/kg body-weight). *Intravenous induction of anaesthesia* Unpremedicated patients: 0.3mg/kg body-weight or more. Premedicated patients: 0.2mg/kg body-weight may be adequate. *Intramuscular premedication* (10mg/2ml ampoule only) Usual dose about 5mg (approx. 0.07-0.1mg/kg body-weight). Elderly patients are more sensitive to the effects of Hypnovel and lower doses should be used. Children over the age of seven years may receive Hypnovel for induction of anaesthesia in a dose of 0.15mg/kg body-weight. **Contra-indications** Benzodiazepine sensitivity; acute pulmonary insufficiency; respiratory depression. **Precautions** Use during pregnancy and lactation should be avoided. Patients should not drive or operate machinery for eight hours after administration. Avoid alcohol. Sedative effects of other centrally-acting drugs may be intensified. For the administration of Hypnovel a second person should alway be present and facilities for resuscitation should always be available. **Side-effects** Hypnovel well tolerated and changes in arterial blood pressure, heart rate and respiration are usually slight. The rapid injection of a high dose can induce soft-tissue airway obstruction or apnoe of short duration. Local effects on veins are infrequent. However, pain on injection and thrombophlebitis may occur. **Presentation** Ampoules containing 10mg midazolam base as t hydrochloride in 5ml or 2ml aqueous solution, in packings of 10. **Basic NHS Cost** 76p per 10mg/5ml ampoule. 64p per 10mg/2ml ampoule. **Product Licence Numbers** 0031/0189 (10mg/5ml), 0031/0126 (10mg/2ml). **Product Licence Holder** Roche Products Limited, PO Box 8, Welwyn Garden City, Hertfordshire AL7 3AY. **Reference** 1. Anaesthesia. 1982, **37,** 1002.
Hypnovel is a trade mark.

ROCHE

J391096/286



ALMIC MEDICAL
DIVISION

E WELLCOME FOUNDATION LTD

With Tracrium there are no cumulative effects with supplemental dosing, so the pattern of block and recovery remains consistent, regardless of the number of doses given.

Surgical muscle relaxation can therefore be conveniently extended at a uniform level for as long as required, simply by repeated incremental bolus doses given at predictable clock-timed intervals or by continuous i.v. infusion.

The rate of recovery remains just as rapid as that seen after administration of a single bolus dose, so reversal can be promptly and easily achieved whatever the duration of the operation – regardless of the patient's age and hepatic, renal and circulatory status.

All of which adds up to an unusual degree of versatility.

That's why more and more anaesthetists are using Tracrium routinely, in procedures of widely differing type and length, from laparoscopy to open-heart surgery.

Wellcome

Muscle relaxation without cumulation.

TRACRIUM

Atracurium besylate

(Prescribing information overleaf.)

*Trade Ma

Tracrium Prescribing Information

Uses Tracrium is a highly selective, competitive (non-depolarising) muscle relaxant for use in a wide range of surgical procedures and to facilitate control of respiration. Tracrium is highly suitable for endotracheal intubation, especially where subsequent relaxation is required.

Dosage and administration

Intravenous injection: Adults and children over 1 year: 0.3-0.6 mg/kg depending on the duration of block required; this will provide relaxation for about 15-35 minutes. Tracrium may be used at standard dosage in elderly patients and in those with respiratory, hepatic or renal failure. Full block can be prolonged with supplementary doses of 0.1-0.2 mg/kg as required. Successive supplementary dosing does not give rise to cumulation. Endotracheal intubation can usually be accomplished within 90 seconds of intravenous injection of 0.5-0.6 mg/kg. The neuromuscular block produced by Tracrium can be rapidly and permanently reversed by standard doses of neostigmine which should be preceded by the administration of atropine. Recovery from full block without the use of neostigmine occurs in about 35 minutes.

Continuous infusion: Tracrium is suitable for administration by continuous infusion at rates of 0.005-0.01 mg/kg/minute (0.3-0.6 mg/kg/hour) to maintain neuromuscular block during long surgical procedures. Tracrium maintains acceptable physical and chemical stability in daylight at concentrations of between 0.5 and 0.9 mg/ml at 30°C for up to: 4 hours in: Compound Sodium Lactate Intravenous Infusion B.P.; 8 hours in: Ringer's Injection U.S.P.; Glucose Intravenous Infusion B.P. 5% w/v; Sodium Chloride 0.18% w/v and Glucose Intravenous Infusion B.P. 4% w/v and up to 24 hours in: Sodium Chloride Intravenous Infusion B.P. Tracrium can be administered by infusion during cardiopulmonary bypass surgery, at the recommended infusion rate. Induced hypothermia to a body temperature of 25 to 26°C reduces the rate of inactivation of atracurium, therefore full neuromuscular block may be maintained by approximately half the original infusion rate at these temperatures.

Contra-indications, warnings, etc. Contra-indicated in patients hypersensitive to atracurium besylate. Tracrium should be used with caution in patients receiving aminoglycosides or polypeptide antibiotics and in patients with myasthenia gravis. In common with all other neuromuscular blocking agents, adequate facilities must be available for endotracheal intubation and artificial ventilation. The neuromuscular block produced by Tracrium may be increased by the concomitant use of inhalational anaesthetics such as halothane. Tracrium should not be mixed in the same syringe with any other agent; in particular it must not be mixed with thiopentone or any alkaline agent, as the high pH would cause inactivation of the Tracrium. As with all other neuromuscular blocking agents the possibility of transient hypotension due to histamine release cannot be excluded. Although animal studies have indicated that Tracrium has no adverse effects on foetal development, nevertheless, like all neuromuscular blocking agents, it should be used with caution in pregnant women. Tracrium may be used to maintain neuromuscular relaxation in Caesarean section as atracurium does not cross the placenta in clinically significant amounts.

Presentation Tracrium injection contains 10 mg per ml atracurium besylate. Two ampoule sizes, 2.5 ml and 5 ml, are available.

Basic NHS costs £6.50 for a box of 5 x 2.5 ml ampoules. £12.50 for a box of 5 x 5 ml ampoules. (PL3/0166).

Further information is available on request.

Calmic Medical Division
The Wellcome Foundation Ltd
Crewe, Cheshire

Wellcome

TRACRIUM
Atracurium besylate

CALMIC MEDICAL DIVISION

ACADEMIC PRESS

publishes books and journals in many areas of Science including:

Acoustics, Agriculture, Anatomy, Anthropology, Archaeology, Audiology

Biochemistry, Biology, Botany

Cancer research, Cardiology, Chemistry, Computer science

Economics, Engineering, Environmental science

Food Science

Geography, Geology

Immunology

Materials technology, Mathematics, Microbiology

Neuroscience, Nutrition

Oncology, Ornithology

Pathology, Pharmacology, Physics, Physiology, Psychiatry, Psychology

Religion

Sociology, Speech, Surgery

Toxicology

Virology

Zoology

BOOKS AND JOURNALS

24-28 Oval Road, London NW1 7DX, U.K.
Orlando, FL 32887, USA.

longitudinally folded gauze swabs and the facemask applied and fixed in the usual way. The gel softens and spreads amongst the facial hair and the fibres of the swabs, forming a gastight seal between the mask and the skin; at the end of the procedure it is removed with a clean swab.

The technique has the advantage of using materials available in every anaesthetic room and is very simple to apply. Furthermore, it is very cheap since several patients can be treated from one tube of gel.

Nuffield Department of Anaesthetics, A.J. MORTIMER
The Radcliffe Infirmary,
Oxford OX2 6HE

Alarming disconnexions

Dr Sury and colleagues (*Anaesthesia* 1986; **41:** 91) have recently suggested for the Servo ventilator 900 series the universal adoption of a mechanical stop which prevents the lower expired minute volume alarm from being set to zero. This modification has clearly proved satisfactory to Dr Sury's department, and has much to commend it, but from discussion with other anaesthetists there may be those who would in certain circumstances find the deliberate inflexibility of the stop a sufficient restriction to forgo its adoption.

There is a flexible method of dissuasion of unauthorised staff not only from turning the lower limit of the expired minute volume alarm to zero, but also from adjusting any of the facia controls on the Servo 900 series. This takes the form of a lightweight, but sturdy transparent plastic cover that hangs in front of the controls, leaving them fully visible. It is suspended by two simple and robust hook-like hinges easily located at the top corners of the face of the ventilator. When necessary, it may be instantly lifted up or completely removed for access to the panel since there are no locking catches. The cover restricts direct access to all the facia controls other than the mute switch and minute volume control for which holes are cut. It thus provides an effective, transparent 'No Entry' sign that reminds prying hands of local policy as to who may and who may not alter the controls; when removed it leaves the controls themselves unmodified.

Dr Sury rightly drew attention to the limitations of the flashing light found on the Servo 900C and 900D models, which is activated when the lower limit alarm is set to zero, but it was perhaps not made clear that this facility is not available on the 900 and 900B models.

Inevitably, the priorities of those responsible for equipment policy are various; in addition, the Servo is often put to use in several environments. This modification, which may be made locally, and has for some time been available from Siemens, should appeal to many departments. Messrs Siemens Ltd would be happy to supply the appropriate details.

Department of Anaesthetics, C.M.S. COOPER
Royal Hallamshire Hospital,
Sheffield S10 2RX

The price of safety—cash too?

A recent report on breathing attachments[1] includes the following statement.

'Worldwide, the growing number of reports of breathing system disconnections, and misconnections has aroused widespread concern over these avoidable incidents. The problem of disconnection is certainly greater than is reported, and probably much greater than imagined. Although the majority may cause no harm to the patient, the results could and have been, in some instances, disastrous.'

The report, in its final recommendations, then misses the opportunity to support strongly the concept of redesigning breathing connexions, and instead recommends close adherence to BS3849 (plug-fit), admittedly a stop-gap for the moment, and suggests that 'Consideration should be given to the routine use of alarms to indicate accidental disconnection or over-pressure in the breathing system'.

A number of points deserve consideration in this context. Unless and until the routine use of an alarm which conforms to an approved pattern becomes medicolegally mandatory, patients will continue to die from accidental and unnoticed disconnection. Anyway, alarms, too, have their problems!

It is impossible to believe that any self-respecting engineer would accept our primitive and dangerous plug-fit connexions for a vital part of his equipment, any more than an electrician would accept the standard laryngoscope blade contact!

Should the Association of Anaesthetists of Great Britain and Ireland in this country consider its official attitude in this context? One of our Defence organisations tells me its view must reflect that of our specialty, since there is no Statute here.

One manufacturer has produced a safety connector, but it is only suitable for the Y-piece. Others, including myself, have designed different safety connexions for specific situations.

Surely some enterprising manufacturer, recognising its market potential, could produce a device which would permit immediate conversion of existing equipment, or most of it, to a safe pattern. Of course, experience in trying to introduce new ideas suggests it will not be a British company! The familiar domestic vacuum cleaner hose connexion already gives one tested approach. The Department of Health has made scavenging systems for anaesthetic gases compulsory, for the health of medical and other staff. How about something now for the patient? As Benjamin Franklin puts it 'would you persuade, speak of interest, not of reason'. Litigation can be very expensive!

National Heart Hospital,
Westmoreland Street,
London W1M 8BA

A. GILSTON

Reference

1. HEALTH EQUIPMENT INFORMATION. Evaluation of breathing attachments for anaesthetic apparatus to BS 3849. 1965. December, 1985.

Design of castors of anaesthetic machines

Scrutiny of the fault histories of anaesthetic machines in this Region shows that a substantial percentage of faults involve the castors. These range from simple problems, such as the wheels jamming, to catastrophic collapse of the castor, resulting in serious damage to equipment. In the latter case, the possibilities of injury to staff and adverse effects to patients are obvious, so we investigated castor loading on a number of machines.

The calculated load on each castor in the case of an anaesthetic machine carrying only medical gas cylinders and anaesthetic accessories, and assuming even weight distribution, is usually around the manufacturer's design limit. When monitoring gear is added, the calculated loading can exceed this limit. For example, a typical weight of a Boyle's 2000 with a modest amount of monitoring equipment gives a load of 50 kg per castor against a design load of 45 kg for light duty applications of that castor.

In reality, the total weight of the machine will generally be distributed unevenly between the castors. This is caused by unavoidable manufacturing inaccuracies in the frame and also by uneven floor surfaces. The load is mainly taken by three castors in the case of a rigid frame and a hard floor. However, two diagonally opposed castors may take the bulk of the load with only a small fraction taken by the third.

This applies even if all four castors seem to be making good contact with the floor. Thus, our measurements show that, in most cases, there is a significantly uneven weight distribution resulting in two of the four castors being loaded well beyond their design limit, even in the absence of monitoring equipment.

We think it important for medical equipment manufacturers to take this into account and specify castors accordingly. We suggest that the following formulae be used. Take the weight of the anaesthetic machine and add 40 kg for monitoring equipment if a shelf is provided on the machine. Multiply this value by 1.2 to take account of the modestly heavy duty cycle to which these castors are exposed. Divide this value by three to arrive at a minimum design load for selecting suitable castors.

It is important that anaesthetists are aware of the loading limitations of machines currently on the market so that accidents may be avoided and manufacturers should also take the action described, so that we can be assured that this equipment is entirely suitable for its purpose.

Department of Clinical Physics
and Bioengineering
11 West Graham Street,
Glasgow G4 9LF

A.J. MUNLEY
A. SHAW

High halothane concentrations from reversed flow in a vaporizer

Reversed flow through a vaporizer such as an Ohmeda Mark III Fluotec produces higher halothane concentrations than indicated on the dial (Table 1). In principle, it should not be possible for a back bar-mounted vaporizer to be connected such that the gas flows in the reverse direction. However, we report on one such occurrence which was due to back bar misconnexion after repair.

The anaesthetic machine was an Ohmeda Boyle's M with a Selectatec back bar. This back bar can accommodate two Selectatec vaporizers, with a switch provided to select either vaporizer. The Ohmeda service engineer replaced this switch after damage and in the course of reconnecting the pipe work, reversed the gas flow to the vaporizers. This machine was in service for approximately one month when a medical physics technician, undertaking a routine check, noticed high vaporizer readings on the Riken interferometer. Subsequently, the problem was resolved by the Ohmeda service engineer.

This incident raises a number of points. This error allowed high concentrations of halothane to be produced, which is potentially hazardous. None of the checks used by Ohmeda (or any other manufacturer's

Table 1. Output concentration of halothane when vaporizer flow (0_2, 5 litres/minute) reversed

Setting of vaporizer (%)	1	1.5	2	3	2	1	0
Reading on Riken interferometer	2.42	3.36	4.24	5.75	4.0	2.34	0+

service agent) detects the halothane concentration and medical physics technicians do not routinely check machines after service visits. The problem was not noticed clinically, which reflects the fact that anaesthetists look at patients rather than dials. The anaesthetic machine in question was being used for maintenance of anaesthesia in the gynaecology theatre, where low concentrations of volatile agents were administered to mostly young, fit, adult patients via a Mapleson A system or Blease Manley ventilator. Had the machine been used in other circumstances, the problems of overdosage and prolonged recovery from anaesthesia might have become apparent, particularly after prolonged administration.

We therefore recommend that this type of back bar be replaced and that change-over switches, whether for anaesthetic agents or for gas outlets, be avoided.

Department of Medical Physics,
Department of Anaesthetics,
Monklands District General Hospital,
Monkscourt Avenue,
Airdrie ML6 OJS

R. RAILTON
M.D. INGLIS

Hazardous tracheal tube pilot balloons

Tracheal tube cuffs are routinely tested by the injection of an arbitrary volume of air into the cuff *in vitro*, and demonstration of its continued distension over a period of time. It is now well recognised that the pressure in a cuff *in vivo* increases gradually as nitrous oxide diffuses into the cuff. Prandt[1] has suggested that cuff pressure is limited by configurational changes in the cuff or the pilot balloon, depending which one has the greater compliance, and states that, in nearly all tubes, the cuff will have the greater compliance.

New tracheal tubes (Leyland, Magill red rubber 8.0 mm I.D.) were tested in the manner described and were subsequently found suddenly to lose their seal *in vivo*, with aneurysmal change in the pilot balloon and obvious clinical risk. This happened some time after the operation had begun; presumably the increase in pressure due to nitrous oxide diffusion caused the pilot balloons to stretch to such a degree that their compliance rose sufficiently to allow the cuffs to empty into them (analogous to Laplace's law).

Testing of the faulty tubes showed that *in vitro* a 12-ml inflation of the cuff system caused no problems. However, when the cuff was put into a mock trachea (20-ml syringe barrel with a 20-mm diameter), the initial cuff inflation was normal but 12 ml caused sudden distension of the pilot balloon and emptying of the cuff.

This sudden cuff emptying occurred at 24 kPa and 29 kPa for two cuffs when measured via a three-way tap with a Druck DPI 100 pressure monitor. These are intracuff pressures which would be reached in normal clinical use of Magill tubes.[2]

Nine other tracheal tubes from the batches of the above tubes, tested in the same way, emptied their cuffs at an average of 65 kPa (range 51–85 kPa), well outside clinical range, and with variable loss of their seal. In addition, this required the unnatural injection volume of 33.8 ml (average 33.8 ml; range 22–40 ml) from a 50-ml syringe with admitted inaccuracy due to compression of air in the syringe. The emptying pressures were consistently lower when tested a second time. Presumably, stretching the pilot balloons once increased their compliance.

These serious effects may be expected in old tubes, with perished rubber in the pilot balloon. The two tubes shown were new, and the matter has been brought to the attention of the supplier.

It is suggested that this serious problem might be prevented if cuffs were routinely tested inside a mock trachea, with a slightly larger than normal volume of air, to simulate the rise in pressure achieved *in vivo*.

Department of Anaesthetics,
Royal Hallamshire Hospital,
Glossop Road,
Sheffield 10

I.H. HERREMA

References

1. BRANDT L. Pressures on tracheal tube cuffs. Some corrections (letter) *Anaesthesia* 1982; **37:** 964–5.
2. BLACK AMS, SEEGOBIN RD. Pressures on endotracheal tube cuffs. *Anaesthesia* 1981; **36:** 498–511.

Disconnexion within an anaesthetic machine

We report on a noisy and potentially serious problem that occurred using a Boyle anaesthetic machine Model M.

A fit patient recently had a surgical procedure in the lithotomy position. Anaesthesia included tracheal intubation and automatic intermittent positive pressure ventilation of the lungs with the Penlon Oxford ventilator. This was driven by an oxygen supply, at approximately 380 kPa, derived from a mini Schraeder outlet on the anaesthetic machine.

The patient was put into the lithotomy position on an Eschmann GXL table. Once she was stable, the orderlies asked permission to move her down by sliding the table along the runners on the table. One of the orderlies gripped the anaesthetic machine along its front edge in order to move it alongside the table, to prevent any tension in the patient breathing system. When he gripped and pulled the machine, there was a loud roaring sound and automatic ventilation stopped. The high pressure oxygen pipeline had been disconnected at a pipeline joint on the machine.

The noise alerted the staff to the problem and whilst an Ambu bag was being brought into theatre the orderly had managed to replace the pipe in the affected joint and was able with force to maintain a gas-tight seal. Another anaesthetic machine was brought into the operating room and the patient was transferred. The patient did not suffer hypoxia due to the alertness of the theatre staff and the operation was concluded successfully.

The machine, which was on a standard maintenance contract with Ohmeda, the manufacturers, was subsequently inspected by the Physics Department and a representative of Ohmeda. The oxygen pipe which had become disconnected supplied oxygen to an auxillary outlet block and was routed along the front edge of the machine directly under the top tray (Fig. 1).

Simplifix compression fittings are used extensively on the Boyle range of anaesthetic machines for pipe jointing. It was apparent that the pipe had been pulled out of one such joint by the force exerted as it was gripped against the front edge of the machine. Further inspection showed that the securing nut at the joint concerned was only finger tight and had never been tightened sufficiently to compress the sealing ferrule onto the tube. Other joints on the machine, whilst not leaking, were in a similar condition.

In view of these findings, the joints at either end of the similarly positioned pipe on seven other anaesthetic machines in the theatre suite were inspected. The torque required to loosen the joints were measured in each case. A mean value of 2.2 Nm (range 1.4–2.7 Nm) was measured for the 14 joints inspected. In each case the sealing ferrules had been properly compressed onto the pipes.

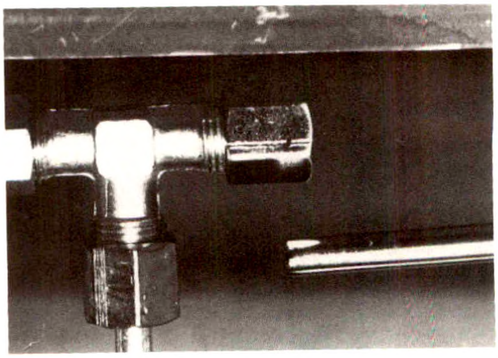


Fig. 1.

This is a potentially serious hazard since disconnexion of high pressure oxygen pipe work on the machine effectively removes the oxygen supply to the Rotameter block which supplies the patient system and to auxillary outlets which may be used to drive ventilators. This supply is not restored by opening the oxygen cylinders attached to the machine.

It is accepted that a handle is provided at one corner of the machine, but in practice users frequently find it more convenient to grip the machine at other locations in order to guide it as it is being moved. The position of a gas supply pipe along, and close to, the front edge of the machine therefore presents a potential hazard. This was exacerbated in the case reported here by the fact that the pipe joints were inadequately tightened (although the machine was regularly serviced under contract). Rerouting the pipe away from the front edge, which appears to present no technical difficulties, would minimise the possibility of accidental damage to the pipeline joints.

This incident has been reported under the Hazard warning system and to the Safety committee of the Association of Anaesthetists of Great Britain and Ireland. It should also be noted that unless an obvious gas leak resulted, the presence of the inadequately tightened securing nuts would not normally be detected by standard user safety procedures.

Department of Anaesthesia, H.M. JONES
Royal Infirmary,
Glasgow G31 3ER
Department of Clinical Physics M.J. SIK
and Bioengineering,
Crosshouse Hospital,
Kilmarnock,
Ayrshire

Flowmeters: an old problem reappears

The plastic bodied oxygen flowmeters produced by Ohmeda Ltd have recently been the subject of a significant number of complaints associated with apparent fluctuation in the gas flow. What usually happened was that the flow was set to 5 litres/minute and then, after a period of time, the reading changed to around 9 litres/minute. If the flow was re-adjusted to give a reading of 5 litres/minute then again after a period of time the reading changed without further adjustment of the control valve. Readings as low as 2 litres/minute were observed. In certain circumstances it was found to be impossible to set a flow of 5 litres/minute. In this case, the indicator ball rises smoothly to around 4 litres/minute and then suddenly jumps to 6 litres/minute with the reverse effect when trying to reduce the flow to 5 litres/minute.

These effects were very frustrating for the staff involved, since it meant that they had to check the flowmeter reading much more frequently. They began to suspect and criticise the control valve on the flowmeter and also the stability of the pressure in the hospital piped gas system. However, investigation quickly revealed that an electrostatic charge was accumulating in the flowmeter and that this was affecting the position of the indicator ball. When this happens the delivered flow is not accurately related to the indicator ball position.

This problem is acute in this particular model of flowmeter, not only because it is made from plastic material which is not antistatic, but also because of the light weight of the indicator ball. This ball weighs only 0.15 g and hence the forces generated by the electrostatic charges can have a significant effect on its position.

The problem may not be too critical where the patient is using a Venturi type face mask as variations in oxygen flow will not have too much effect on the concentration of oxygen delivered. However, the effect significantly alters oxygen concentration in most other forms of oxygen therapy; in these circumstances we strongly suggest that alternative flowmeters be used.

West of Scotland Health Boards,
Department of Clinical Physics
and Bio-Engineering,
11 West Graham Street,
Glasgow G4 9LF

W. Richardson
A. Shaw

Protective sheath for nasotracheal tube

A progressive level of sterility marks the respiratory tract distal to the vocal cords, whereas the upper airways are known to be abundantly populated with potentially pathogenic bacteria.[1] Tracheal intubation is believed to be responsible for the transfer of bacteria, especially when the nasal route is used.[2,3] Recently, a protective hood has been devised for mechanical purposes.[4] A simple protective sheath to minimise the bacterial contamination caused by a nasotracheal tube might also be useful.

Twenty-five adult patients, for cholecystectomy or gastric resection under general (halothane) anaesthesia, were randomly divided into two groups. In the first group of 10 patients, unprotected tubes were used; in the remainder sheathed tubes were used. The sheaths were improvised from very thin, but tough, sheets of polyethylene; they were as long as the tube and 2–3 cm in diameter. They were sterilised together with the tracheal tubes by ethylene oxide in protective bags (Fig. 1).

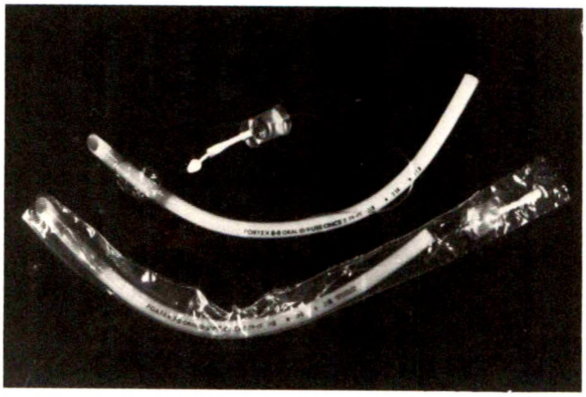


Table 1.

	Cases with identical flora		Probability
	Unprotected tubes	Protected tubes	
Tube cuff/nose	10/10	5/15	<0.0005
Tube tip/nose	6/10	3/15	<0.05

The nasal fossa, epipharynx and tracheal walls (through the glottis) were sampled for bacteriological examination before tracheal intubation. After the sheathed tube reached the epipharynx, just close to the glottis, a hood was cut out from the sheath end, corresponding to the tube tip, with long scissors. It was only then that, with Magill forceps, the tube was passed further into the trachea by sliding it within its sheath. Once anaesthesia finished, tracheal extubation under direct vision control, and after careful toilet of the pharynx, was performed. When the cuff and the end of the tube appeared in the pharynx, they were sampled for bacteriological examination. Sheaths, tubes, instruments and suction catheters were all sterile before use.

The cultures were considered in relation to the bacteria which are normally found in the nasal fossa. These were compared with the cultures from the tracheal portion of the tube and the tip of the tube. The incidence of identical bacterial specimens is shown in Table 1. The sheath offers significant protection.

Nasotracheal intubation with such a tube-in-sheath is more difficult than usual. It might perhaps be reserved for those patients who require ventilatory assistance, but who are considered to have a low natural resistance. Manufacturers could find technical solutions to make it more practical. A removal mechanism for the hood, similar to that of the upper cellophane covering a cigarette packet, i.e. a tear-strip, might be considered.

Spitalul Cl. Judetean,
Str. Clinicilor 3,
3400 Cluj-Napoca 4,
Romania

E. CARDAN
J. VLAD

References

1. DUBOS RJ, HIRSCH JG (Eds). *Bacterial and mycotic infections in man*, 4th edn. London: Pitman Med. Publ. Co. Ltd., 1965, p. 326.
2. BRYANT LR, TRINKLE JK, MOBIN-UDDIN K, BAKER J, GRIFFEN JR WO. Bacterial colonization profile with tracheal intubation and mechanical ventilation. *Archives of Surgery* 1972; **104:** 647–51.
3. VAN UFFELEN R, VAN SAENE HKF, VAN FIDLER V, LOWENBERG A. Oropharyngeal flora as a source of bacteria colonizing the lower airways in patients on artificial ventilation. *Intensive Care Medicine* 1984; **10:** 233–7.
4. HANSEN J, REINHOLD P, WENDT M, STOLL W. Cuffschutz bei nasotrachealer Intubation. *Anaesthetist* 1984; **33:** 384–6.

Peripheral circulation

Dr P.W. Duncan's letter (*Anaesthesia* 1986; **41:** 88) demonstrates the value of a photoelectric pulse monitor as a monitor of regional perfusion in an extremity. This device can also be useful in the acute management of fractures which jeopardise the arterial supply to a limb. A supracondylar fracture of the humerus, in particular, can damage the brachial artery and later manipulations with flexion of the elbow can further compromise perfusion. Both situations may result in Volkmann's ischaemic contracture if not rapidly corrected.[1,2] Thus, great care must be taken to ensure the adequacy of perfusion distal to the injury.

In three separate cases of supracondylar fractures in children it has been found helpful to have a pulse monitor (Kontron finger pulse sensor with a Roche 108 monitor) on the thumb of the injured arm during reduction of the fracture and the subsequent positioning and immobilisation of the limb. The extent to which reducing the fracture improves perfusion can be demonstrated, and the arm can be immobilised with the degree of elbow flexion at which the pulse amplitude is maximal.

This technique is of greatest value when the extent of tissue oedema, swelling and arterial spasm is such that the radial pulse is difficult to assess at all by palpation.

Nuffield Department of Anaesthetics,
John Radcliffe Hospital,
Headington,
Oxford OX3 9DU

C.M. WAIT

References

1. KLINGENSMITH W, OLES P, MARTINEZ H. Fractures with associated blood vessel injury. *American Journal of Surgery* 1965; **110:** 849–52.
2. GOSSLING HR, PILLSBURY SL. *Complications of fracture management*. Philadelphia: JB Lippincott and Company, 1984.

Anaesthesia by telephone: an aid to induction of anaesthesia in children

A popular method for the induction of anaesthesia in children involves the inhalation of gaseous anaesthetic agents. This requires the use of a conventional mask and anaesthetic system which may arouse both fear and suspicion in young patients. Children between the ages of 3 and 6 years pose a very special problem. Indeed, many will respond vigorously even before anaesthetic agents are introduced and physical restraint may then

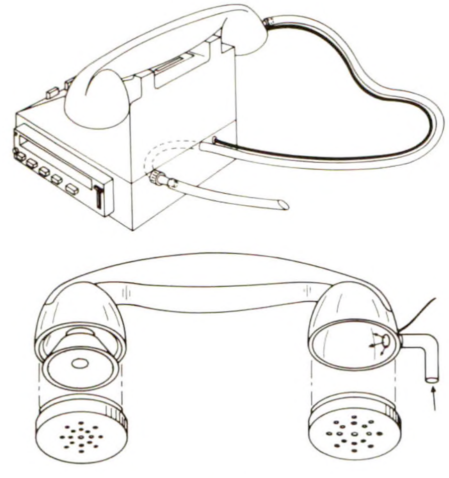


Fig. 1.

be required, with the attendant risk of emotional damage to the child. Patient compliance can be improved by the use of an anaesthetic delivery system which resembles some familiar object, and also by diverting the child's attention to some pleasant subject. Bigger children, babies and neonates are usually not a problem for induction of anaesthesia.

We have modified a toy telephone for induction of anaesthesia in pre-school children. (Fig. 1). A gas delivery tube and a telephone speaker are fitted to the mouthpiece and earpiece respectively and a tape recorder is placed within the instrument base. By this means, nursery stories can be heard by the patient while holding the telephone to his ear. In this position anaesthetic gases can easily be added to his inspired air.

Initially, the device is introduced to the child as a friendly toy, preferably on the day before surgery. At that time a clear, truthful and appropriately detailed account is given to the child as to the exact function of the anaesthetic telephone.

Special care is taken that the child and his parents understand clearly that the telephone functionally resembles the conventional mask, but just makes it easier and more pleasant to hold and that he need not fear physical restraint with a mask. Children are correctly selected at the premedication visit and alternative methods of induction (e.g. intramuscular induction agents) are planned for older children, babies and noncompliant children.

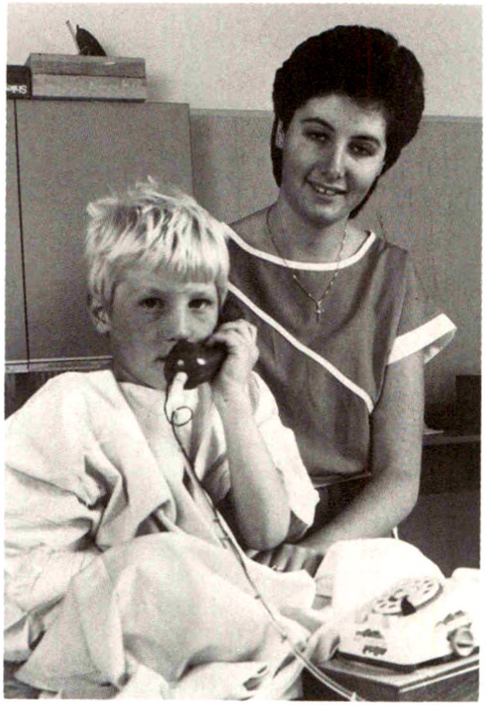


Fig. 2.

Just before induction, the child and his parent(s) are invited into a suitable induction room, the patient is given the telephone again and a story appropriate to the age and sex of the child is selected. Staff and lighting are limited to a safe minimum and physical contact between the child and his parent(s) is encouraged while the staff keep a low profile and the anaesthetic equipment is placed behind the child. Nitrous oxide and oxygen are given from the outset (Fig. 2), with the addition of halothane when drowsiness develops. Upon loss of consciousness, anaesthesia is continued using a conventional anaesthetic breathing system.

In practice the device has proved both effective and popular in young patients. A familiar object such as a toy telephone, and the presence of one or both parents at the time of induction provides the security so badly needed in an otherwise strange environment.

Department of Anaesthesia,
Area 361,
Johannesburg Hospital,
Private Bag X39,
2000 Johannesburg,
South Africa

A.P. Boezaart
C.H. van Hasselt

The anaesthetic pacifier for induction of anaesthesia

The classical babies dummy or pacifier has been used for centuries to quieten unhappy infants. The anaesthetic pacifier, (TLT Instruments Ltd) incorporates a method of administration of anaesthetic gases via such a pacifier. Its effectiveness in induction of anaesthesia was compared to a Rendell-Baker-Soucek type mask (Fig. 1).

Sixty children, aged 1–18 months participated; all

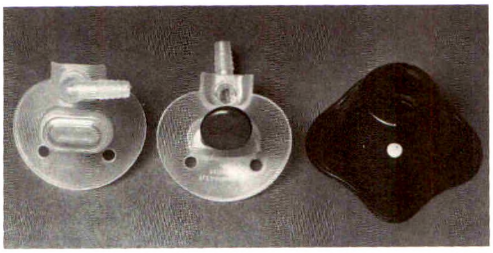


Fig. 1. The anaesthetic pacifier, anterior and posterior views. The nasal hood and gas entry part are shown superiorly. A number 1 Rendell-Baker Soucek Mask is shown for comparison.

were ASA grade 1 or 2. Selection into group A (pacifier) or group B (mask) was on an alternating basis until each group had 30 patients. The two groups were comparable: group A, mean age 7.03 months (SEM 0.869), mean weight 7.8 kg, (SEM 0.457) and group B mean age 7.66 months (SEM 0.786), mean weight 8.0 kg (SEM 0.383).

All the patients received an oral premedication of trimeprazine tartrate 2 mg/kg, methadone 0.1 mg/kg and atropine 0.02 mg/kg intramuscularly before induction 60 minutes. Group A were offered the pacifier in the holding room. If they rejected it, it was dipped in sugar and re-offered. Five out of 35 babies refused the pacifier and were excluded from the study. Induction took place with an oxygen flow of one litre/kg with halothane 4%.[1] The anaesthetist's hand was cupped over the nose hood of the pacifier to act as a reservoir, and the pacifier was gently moved in the mouth to stimulate sucking. Once asleep, muscle tone was lost and the pacifier was displaced; airway obstruction from the tongue frequently occurred. This required placement of a Guedel airway and the use of a Rendell-Baker-Soucek mask. Tracheal intubation was carried out when possible, using the appearance of a fixed central pupil as an end point. The time from commencing induction until intubation was noted. Group B received 4% halothane in oxygen induction via a Rendell-Baker-Soucek mask and Ayre's T-piece.[2] The time to intubation was noted.

Intubation time was faster in group B, mean 2.9 minutes (SEM 0.129), than in group A, mean 3.9 minutes (SEM 0.129). Behaviour at induction was assessed and no differences were shown. Breathholding, defined as longer than 10 seconds, and irregular breathing occurred in five group B patients and in none of the group A patients. It was transitory and of no clinical significance. Salivation was not significant in either group and no laryngospasm occurred.

The anaesthetic pacifier was not suitable for maintenance of anaesthesia because of the loss of a safe airway once the child is asleep; ventilation cannot be assisted with this apparatus. The system is an open one which does not contribute any apparatus dead space but, due to its open nature, does contribute to pollution.

Department of Anaesthesia,
Tygerberg-Hospital,
Private Bag,
Tygerberg 7505,
South Africa

K.A. Payne

References

1. Long EC, Hull WE. Respiratory flow in the crying newborn infant. *Pediatrics* 1961; **27:** 373–7.
2. Brown TCK, Fish GC. *Anaesthesia for children.* Oxford: Blackwell Scientific Publications, 1979; p. 113.

Pneumothorax following insertion of a nasogastric tube

A 66-year-old lady weighing 35 kg, suffering from acute on chronic bronchitis, had been intubated and her lungs ventilated intermittently for 10 days. She was weaned with difficulty. Some hours after tracheal extubation an 85-cm fine bore Clinifeeding Tube with its introducer guide wire was passed without resistance by the nasal route. The patient remained alert and comfortable during the 2 hours whilst a portable radiograph was arranged. Before the developed X ray was returned, she became acutely dyspnoeic and cyanosed with profound bradycardia during physiotherapy. Her trachea was again intubated. The feeding tube was found to pass between the cords and the trachea was deviated to the left. A right-sided tension pneumothorax was drained in the usual way. The patient subsequently made a full recovery.

The portable radiograph clearly showed the feeding tube passing down the right main bronchus and out into the posterior pleural space where the excess tube coiled up. This demonstrates that the reflexes which guard the respiratory tract may be reduced following prolonged tracheal intubation, and emphasises the importance of having a chest radiograph before nasogastric feeding is started.

Colchester General Hospital,
Colchester,
Essex CO4 5JL

W.H. Konarzewski
G.D.H. Richards
S.J. Thomson

The Bridgend modification of the Manley ventilator

The Manley ventilator is one of the most widely used ventilators in operating theatres in Britain. Its ease of use and proven reliability has made it the choice of many anaesthetists. The Bridgend modification is designed to improve upon the original by providing an extra mode of use: controlled ventilation with either a rebreathing or nonrebreathing system.

Figure 1 shows the Blease Manley MP3 which has undergone the Bridgend modification. A variable flow restrictor, labelled *rate* is attached to the right side of the ventilator. This controls the flow from a high pressure air or oxygen supply at 350 to 400 kPa to the conventional 60 kPa gas inlet. This independent gas supply provides the motive force for the ventilator. In use as a driving (power) system with a rebreathing or nonrebreathing system, the inspiratory and expiratory ports are short-circuited by a T-piece and the third limb connected to the breathing system of choice (Fig. 2). This tubing provides a dead space greater than one litre and so the driving gas of the ventilator does not contaminate the patient's breathing system. The tidal volume is set by conventional means. The ventilation rate is dependent upon the gas flow into the ventilator and is adjusted by the flow restrictor labelled *rate*. In

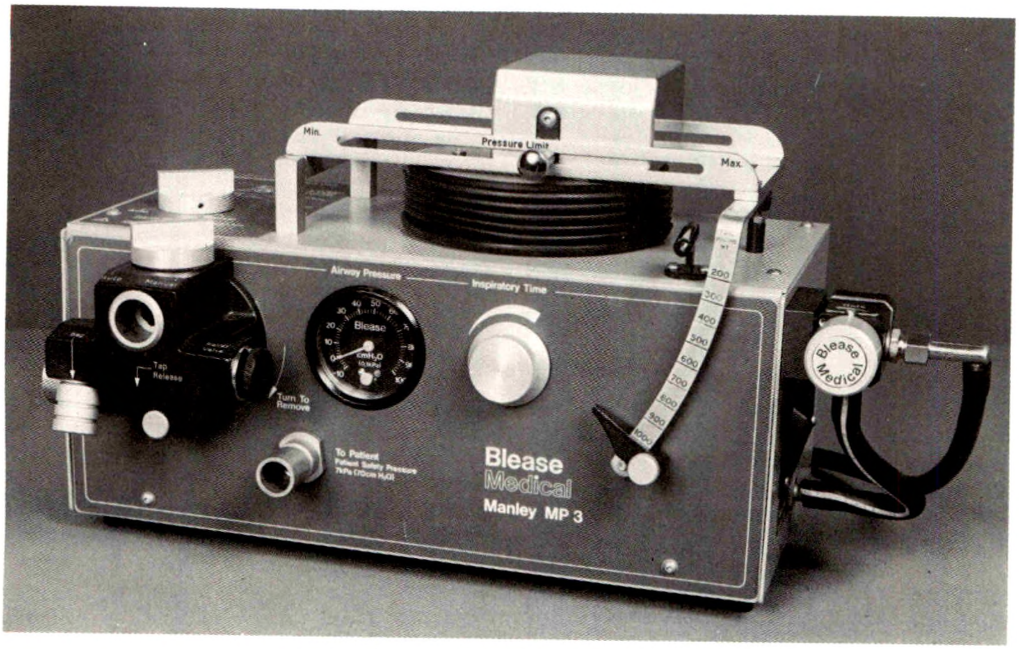


Fig. 1. The Bridgend modification.

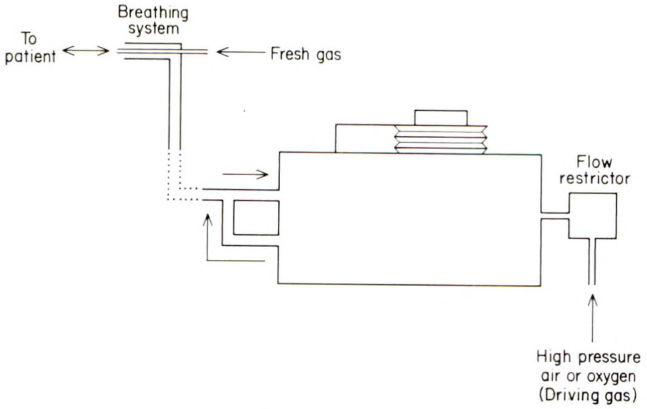


Fig. 2. Flow diagram.

this configuration, the functional characteristics of the ventilator are that of a variable frequency, variable phase, time-cycled, pressure or volume limited pressure generator.

The Bridgend Manley is as easy and reliable in operation as its esteemed progenitor. The added features considerably increase the versatility of the ventilator. As with every anaesthetic system, care has to be taken to ensure the correct connexion of all tubing. The production machine, the Blease Manley 4, of which ours is a prototype, is suitably modified and marked to avoid incorrect use.

We are grateful to Blease Medical Equipment Limited for their technical support and engineering expertise.

Department of Anaesthetics,
Princess of Wales Hospital,
Bridgend,
Mid Glamorgan CF31 1RQ

J.Y. Kwan
R.W. Morris

The case for dilution of ketamine

Ketamine has been used for the past 4 years for radiotherapy in children. Recently, a 3½-year-old child who weighed 16 kg with an astrocytoma was scheduled for planning, mould and radiotherapy.

He had an anaesthetic with ketamine for his first treatment and required 3–4 mg/kg body weight through his Hickman line, which had been inserted previously. The total dose was 50 mg, but within seconds of this injection, the child started screaming and complained that he had a very unpleasant taste in his mouth; he refused to have any treatment the following day. It was decided to dilute the ketamine with normal saline 50 mg in 5 ml and this was given slowly intravenously; the child tolerated the rest of the treatment fairly well without further complaints. Top-up doses of 10–20 mg of ketamine during the radiotherapy procedure were not diluted. The induction dose was diluted and this varied daily from 120–150 mg in subsequent treatments.

Has anyone else had a similar experience?

The Royal Marsden Hospital,
Fulham Road,
London SW3 6JJ

M.K. Gademsetty

The Afya anaesthetic system

The evaluation of the Afya anaesthesia system by E.A. Swai, A.M. Brooks and J.S. Mecklenburgh (*Anaesthesia* 1985; **40:** 1213–6) was interesting. A system which can help to give simple controlled anaesthesia where more complicated machines are either not available or cannot be used, is welcome.

It appears that the Afya vaporizer works on the same basic principles as the EMO but the compensation for temperature changes is different. It is good that it can be used with an Oxford Miniature vaporizer and, indeed, one or two of these could be used instead of the Afya as in the Triservice system.[1]

Is it correct to infer from their Fig. 1 that in the paediatric arrangement, there is a small bag for babies and small children? How vulnerable is the thermometer? It looks as if it might be easy to break. A self-inflating bag is fine for controlled ventilation, but a minor drawback during spontaneous ventilation is that no movement of the bag will be seen. It is here that the Oxford inflating bellows has an advantage. A large proportion of anaesthetics in developing countries employ spontaneous ventilation since expertise in controlled ventilation is rarely available. How will the bag stand up to tropical conditions?

For the benefit of those who have an EMO/OMV system already, it should be pointed out that infants and children can still be managed.[2] Dr Swai mentions either the use of a high gas flow through the vaporizer or the Farman entrainment system; both are possible, but neither are very practicable in situations where gases are in short supply or even not available. However, if an ordinary Ayre's T-piece is used, fitting the gas supply tubing to the Oxford bellows (or bag) outlet then slow repeated compression of the bellows (or bag) will produce a nearly continuous flow of gases to the T-piece. If a simple ventilator such as the positive pressure Radcliffe were to be used to inflate the bellows (*not* the patient) with the anaesthetic gases, the bellows will remain fully expanded and the pressure can produce a flow of 5–10 litres/minute with ease. The set-up is then virtually the same as it would be using a Boyle's machine, but I have no experience of using a self-inflating bag with a ventilator in this way.

Lewisham Hospital,
London SE13 6LH

F.N. Prior

References

1. Houghton IT. The Triservice anaesthetic apparatus. *Anaesthesia* 1981; **36:** 1094–108.
2. Prior FN. Anaesthesia—paediatric priorities. *Africa Health* (Times House, Times Square, Sutton, SM1 4AK, U.K.), 1985. April/May.

A reply

We thank Dr Prior for his observations on our paper.

There is a separate small bag for use with the paediatric system. The thermometer is encased in a tough plastic housing which protects it. We have never had any qualms about its vulnerability. We agree that during spontaneous ventilation the self-inflating bag would show little, if any, movement. However, the disc of the connecting valve is clearly visible through a transparent dome and provides an indication of inspiratory gas flow through the vaporizer. We have no information on the durability of the bags under tropical conditions, but would speculate that it would be no worse than the Oxford inflating bellows.

Modification of the Afya system for use with infants or children is not necessary. Moreover, the use of a Radcliffe ventilator, as described, does sound a rather cumbersome arrangement (if not explosive!).

Department of Anaesthetics, A.M. BROOKS
University Hospital of Wales, J.M. MECKLENBURGH
Cardiff CF4 4XW

A resuscitation box for every anaesthetist?

We agree with Dr Hilton's idea that every anaesthetist should carry resuscitation equipment (*Anaesthesia* 1985; **40:** 486–7) but consider that the needs of the enthusiast and the ordinary anaesthetist should be distinguished. Dr Hilton's box is appropriate for the enthusiast; one intended for every anaesthetist to have in their car, with a likely usage of once every 10 years, should be much simpler.

The primary functions of an anaesthetist at an accident are to maintain the airway, the ventilation and the circulation. Secondary considerations such as analgesia and splintage can be deferred until Entonox apparatus and other ambulance equipment arrives. The extent of these primary functions is open to interpretation. For example, chest drainage could be included within the maintenance of ventilation. Whether or not a chest drain is to be carried can be considered in relation to the likelihood of its being needed. If the chance of meeting a significant injury is once in 10 years, the chance of requiring a chest drain at the roadside would probably be less than once every 100 years. It could therefore be argued that a chest drain is not mandatory equipment for every anaesthetist. For the enthusiast, who has either altered this likelihood by frequent attendance at accidents on a call-out scheme, or who wishes to feel prepared for all eventualities despite the very low probability of meeting them, then chest drainage equipment may be appropriate.

All equipment can be evaluated in this way, with the ordinary anaesthetist focusing on relatively common problems. A corollary is that the broader focus of the enthusiast must not overlook common problems. Thus, both sets of equipment should include frequently needed items such as scissors, a venous tourniquet to help secure venous access and pads to control external bleeding, all omitted from Dr Hilton's list.

The exact choice of equipment is, ultimately, personal. Simplicity is a prerequisite for the occasional attender at accidents. The more comprehensive array of the enthusiast must also retain considerable simplicity if it is to be practical in a dimly lit roadside ditch in winter. Furthermore, the enthusiast should arrange appropriate finance for his kit, and should display sufficient clinical maturity to use equipment only if there is a clear indication. There is little excuse for causing delays in hospital transfer or for carrying out nonessential procedures in the far from ideal conditions of the roadside.

Department of Anaesthetics, P.A. OAKLEY
Princess Margaret Hospital, M. O'CONNOR
Swindon SN1 4JU

A reply

It is pleasing that Dr Oakley and Dr O'Connor agree with my suggestion that every anaesthetist should carry resuscitation equipment, but cannot accept that my box is appropriate for the enthusiast . . . and should be much simpler.

Its aim is to provide, in the smallest possible space, the basic drugs and equipment necessary for an *anaesthetist* to deal with *any* life threatening emergency, not just roadside trauma. Replacing a simple chest drainage system with scissors, a venous tourniquet and pressure pads would add greatly to the bulk, but not much to the chances of survival.

If by enthusiast they mean a doctor using the unique skills of his specialty, to do his best for critically ill patients, then I confess that I am one. Surely anaesthetists can do more than act as glorified first aiders?

Department of Anaesthetics, P.J. HILTON
University Hospital of Wales,
Cardiff CF4 4XW

Anaesthesia, 1986, Volume 41, pages 682–687

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for December 1985. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennyslvania, USA.

Abdominal surgery

Measurement of hepatic blood flow. JOHNSON, D.J., MUHLBACHER, F., WILMORE, D. *Journal of Surgical Research* 1985; **39:** 470.

Mechanisms and role of intrinsic regulation of hepatic arterial blood flow: hepatic arterial buffer response. LAUTT, W.W. *American Journal of Physiology* 1985; **249:** G549.

Gastrointestinal somatostatin: distribution, secretion and physiological significance. MCINTOSH, C.H.S. *Life Sciences* 1985; **37:** 2043.

Effects of hyperventilation and hypoventilation on stress-induced intestinal vasoconstriction. WINSO, O., BIBER, B., MARNER, J. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 726.

Pharmacology

Adrenergic drugs and their antagonists

Cooling and alpha 1- and alpha 2-adrenergic responses in cutaneous veins: role ot receptor reserve. FLAVAHAN, N.A., LINDBLAD, L.-E. *et al. American Journal of Physiology* 1985; **249:** H950.

Anaesthetic agents

Halothane hepatitis: detection of a constitutional susceptibility factor. FARRELL, G., PRENDERGAST, D., MURRAY, M. *New England Journal of Medicine* 1985; **313:** 1310.

Failure of naloxone to reverse the nitrous oxide-induced depression of a brain stem reflex: an electrophysiologic and double-blind study in humans. WILLER, J.C., BERGERET, S. *et al. Anesthesiology* 1985; **63:** 467.

Analgesic agents

Clinical evaluation of a naltrexone sustained-release preparation. CHAING, C.N., HOLLISTER, L.E. *et al. Drug and Alcohol Dependence* 1985; **16:** 1.

Morphine initiates migrating myoelectric complexes by acting on peripheral opioid receptors. TELFORD, G.L., HOSHMONAI, M. *et al. American Journal of Physiology* 1985; **249:** G557.

Meptazinol—a cause of respiratory depression in general anaesthesia. WILKINSON, D.J., O'CONNOR, S.A. *et al. British Journal of Anaesthesia* 1985; **57:** 1077.

Pharmacokinetics and pharmacodynamics of subcutaneous morphine pellets in the rat. YOBURN, B.C., CHEN, J. *et al. Journal of Pharmacology and Experimental Therapeutics* 1985; **235:** 282.

Muscle relaxants

Neostigmine increases the size of subunits composing the quantum of transmitter release at mouse neuromuscular junction. CARLSON, C.G., KRIEBEL, M.E. *Journal of Physiology* 1985; **367:** 489.

Effects of hycanthone on neuromuscular transmission. ENOMOTO, K., EDWARDS, C. *European Journal of Pharmacology* 1985; **116:** 81.

Effect of renal failure on laudanosine excretion in man. FAHEY, M.R., RUPP, S.M. *et al. British Journal of Anaesthesia* 1985; **57:** 1049.

Other drugs

Effect of diazepam on drug absorption and gastric emptying in man. ADELHOJ, B., PETRING, O.U. *et al. British Journal of Anaesthesia* 1985; **57:** 1107.

Apparatus

Clinical assessment of oxygen conserving devices in chronic bronchitis and emphysema. GOULD, G.A., HAYHURST, M.D. *et al. Thorax* 1985; **40:** 820.

Technical and clinical assessment of oxygen con-

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London, WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. An exact copy of the monthly section or various cumulative classifications of the Anaesthetic Literature published in the Journal can be obtained on application to him. References from January 1984 have been entered on data base and search facilities are also available. All communications about this matter should be addressed to Dr Kaufman please.

centrators. GOULD, G.A., SCOTT, W. *et al. Thorax* 1985; **40:** 811.

Facilitated blind intubation using a transtracheal guide wire. HESLET, L., SAND CHRISTENSEN, K. *et al. Danish Medical Bulletin* 1985; **32:** 275.

Evaluation of six oxygen concentrators. JOHNS, D.P., ROCHFORD, P.D., STREETON, J.A. *Thorax* 1985; **40:** 806.

An oxygen conserving nasal cannula. MOORE-GILLON, J.C., GEORGE, R.J., GEDDES, D.M. *Thorax* 1985; **40:** 817.

Behavior and extradural pressure monitor: comparison of extradural with intraventricular pressure in acute and chronically raised intracranial pressure. POWELL, M.P., CROCKARD, H.A. *Journal of Neurosurgery* 1985; **63:** 745.

Hazards of glass ampoules. SHAW, N.J., LYALL, E.G.H. *British Medical Journal* 1985; **291:** 1390.

Conservation of oxygen supply using a reservoir nasal cannula in hypoxemic patients at rest and during exercise. SOFFER, M., TASHKIN, D.P. *et al. Chest* 1985; **88:** 663.

Complications

Oxygen free radical induced damage in kidneys subjected to warm ischemia and reperfusion: protective effect of superoxide dismutase. BAKER, G.L., CORRY, R.J. *et al. Annals of Surgery* 1985; **202:** 628.

True vocal cord paralysis following intubation. CAVO, J.W. *Laryngoscope* 1985; **95:** 1352.

Familial vocal cord dysfunction. CUNNINGHAM, M.J., EAVEY, R.D., SHANNON, D.C. *Pediatrics* 1985; **76:** 750.

Burns. DEMLING, R.H. *New England Journal of Medicine* 1985; **313:** 1389.

The consequences of a cavalier approach to central venous catheterization. HOSHAL, V.L., ARBOR, A. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 11 (Suppl 81).

Acute tetrachloroethylene poisoning—blood elimination kinetics. KOPPEL, C., ARNDT, I. *et al. Journal of Toxicology. Clinical Toxicology* 1985; **23:** 103.

Fluorocarbons: a potential treatment of cerebral air embolism in open-heart surgery. MENASCHE, P., PINARD, E. *et al. Annals of Thoracic Surgery* 1985; **40:** 494.

Possible mechanisms for mianserin induced neutropenia associated with saturable elimination kinetics. O'DONNELL, J.L., SHARMAN, J.R. *et al. British Medical Journal* 1985; **291:** 1375.

Drug-induced hyperkalemia. PONCE, S.P., JENNINGS, A.E. *et al. Medicine* 1985; **64:** 357.

Paraplegia following epidural anesthesia. A case report and a literature review. SKOUEN, J.S., WAINAPEL, S.F., WILLOCK, M.M. *Acta Neurologica Scandinavica* 1985; **72:** 437.

Hypoxemia after gastric bypass surgery for morbid obesity. TAYLOR, R.R., KELLY, T.M. *et al. Archives of Surgery* 1985; **120:** 1298.

General anaesthetic procedures

Anaesthetising the asthmatic. MORGAN, C., GILLBE, C. *British Journal of Hospital Medicine* 1985; **34:** 326.

General interest

Pheochromocytoma—operative surgery. CULLEN, M.L., STAREN, E.D. *et al. Surgery* 1985; **98:** 927.

Myocardial infarct size and mortality in diabetic patients. GWILT, D.J., PETRI, M. *et al. British Heart Journal* 1985; **54:** 466.

Comprehensive pharmaceutical services in the surgical suite and recovery room. KEICHER, P.A., MCALLISTER, J.C. *American Journal of Hospital Pharmacy* 1985; **42:** 2454.

'It's better to be smart than dumb' or the clinical importance of ignorance. LEE, R.V. *American Journal of Medicine* 1985; **79:** 548.

Cardiac involvement in myotonic muscular dystrophy. MOORMAN, J.R., COLEMAN, R.E. *et al. Medicine* 1985; **64:** 371.

Circadian variation in the frequency of onset of acute myocardial infarction. MULLER, J.E. *et al. New England Journal of Medicine* 1985; **313:** 1315.

Direct blood pressure monitoring in patients with pheochromocytoma. NOMURA, A., YASUDA, H., KATO, K. *et al. Japanese Heart Journal* 1985; **26:** 845.

Diagnosis and natural history of Ebstein's anomaly. RADFORD, D.J., GRAFF, R.F., NEILSON, G.H. *British Heart Journal* 1985; **54:** 517.

Local analgesia

Phase distribution studies on an oil–water emulsion based on a eutectic mixture of lidocaine and prilocaine as the dispersed phase. NYQVIST-MAYER, A.A., BRODIN, A.F., FRANK, S.G. *Journal of Pharmaceutical Sciences* 1985; **74:** 1192.

Spinal and epidural analgesia

Systemic morphine enhances spread of sensory analgesia during postoperative epidural bupivacaine infusion. LUND, C., MOGENSEN, T. *et al. Lancet* 1985; **2:** 1156.

Spinal opioids

Distribution of morphine and meperidine after intrathecal administration in rat and mouse. GUSTAFSSON, L.L., POST, C. *et al. Anesthesiology* 1985; **63:** 483.

The Sir Henry Dale lecture of 1985: endogenous opioids and related peptides: from molecular biology to clinical medicine. Imura, H., Kato, Y. *et al. Journal of Endocrinology* 1985; **107:** 147.

Delayed respiratory depression following extradural injection of morphine. Leykin, Y., Ruddick, V. *et al. Israel Journal of Medical Sciences* 1985; **21:** 855.

Endogenous opiates: 1984. Olson, G.A., Olson, R.D., Kastin, A.J. *Peptides* 1985; **6:** 769.

Desensitization to substance P following intrathecal injection. A technique for investigating the role of substance P in nociception. Sawynok, J., Robertson, G. *Archives of Pharmacology* 1985; **331:** 152.

Obstetric anaesthesia and analgesia

Fetal subcutaneous scalp PO_2 and abdominal heart rate during labor. Aarnoudse, J.G., Huisjes, H.J. *et al. American Journal of Obstetrics and Gynecology* 1985; **153:** 565.

Comparative maternal and neonatal effects of halothane and enflurane for Caesarean section. Abboud, T.K., Kim, S.H. *et al. Acta Anaesthesiologica Scandinavica* 1985; **29:** 663.

The influence of antecedent renal disease on pregnancy. Abe, S., Amagasaki, Y. *et al. American Journal of Obstetrics and Gynecology* 1985; **153:** 508.

Epidural analgesia during labour: why does this increase the forceps delivery rate? Bates, R.G., Helm, C.W. *Journal of the Royal Society of Medicine* 1985; **78:** 890.

Obstetric haemorrhage: causes and management. Boulton, F.E., Letsky, E.A. *Clinics in Haematology* 1985; **14:** 683.

Safety of labor and delivery in women with mitral valve prolapse. Chapiro, E.P., Trimble, E.L. *et al. American Journal of Cardiology* 1985; **56:** 806.

Pregnancy in sickle cell disease. Charache, S., Niebyl, J.R. *Clinics in Haematology* 1985; **14:** 729.

Thromboembolism in pregnancy. De Swiet, M. *Clinics in Haematology* 1985; **14:** 643.

Urinary function during epidural analgesia with methadone and morphine in post-Caesarean section patients. Evron, S., Samueloff, A. *et al. Pain* 1985; **23:** 135.

Continuous epidural analgesia for vaginal delivery in Sweden. Report of a nationwide inquiry. Hanson, B., Matouskova-Hanson, A. *Acta Anaesthesiologica Scandinavica* 1985; **29:** 712.

Postpartum cardiomyopathy and acute myocarditis. Huerta, E.M., Erice, A. *et al. American Heart Journal* 1985; **110:** 1079.

Blood volume changes in normal pregnancy. Hytten, F. *Clinics in Haematology* 1985; **14:** 601.

Current concepts: hepatitis in pregnancy. Snydman, D.R. *New England Journal of Medicine* 1985; **313:** 1398.

The effect of oxytocin infusion on uterine activity levels in slow labour. Steer, P.J., Carter, M.C., Beard, R.W. *British Journal of Obstetrics and Gynaecology* 1985; **92:** 1120.

Pre-eclampsia, eclampsia with hemolysis, elevated liver enzymes, and thrombocytopenia. Weinstein. L. *Obstetrics and Gynecology* 1985; **66:** 657.

Paediatric anaesthesia and intensive care

Motility and arousal in near miss sudden infant death syndrome. Coons, S., Guilleminault, C. *Journal of Pediatrics* 1985; **107:** 728.

Uptake of volatile anaesthetics in children. Gallagher, T.M., Black, G.W. *Anaesthesia* 1985; **40:** 1073.

Cardiovascular manifestations of sickle cell anaemia in children. Girardet, J.P. *La Presse Medicale* 1985; **14:** 1963.

Modulation of brain development by morphine: effects on central motor system and behavior. Handelmann, G.E., Dow-Edwards, D. *Peptides* 1985; **6:** 29 (Suppl 2).

Insulin and glucagon during the perinatal period: secretion and metabolic effects on the liver. Ktorza, A., Bihoreau, M.-T. *et al. Biology of the Neonate* 1985; **48:** 204.

Esophageal atresia. Martin, L.W., Alexander, F. *Surgical Clinics of North America* 1985; **65:** 1099.

Hormonal and metabolic changes in the perinatal period. Mayor, F., Cuezva, J.M. *Biology of the Neonate* 1985; **48:** 185.

Obstetric management and diagnosis of haematological disease in the fetus. Nicolaides, K.H., Rodeck, C.H., Mibashan, R. *Clinics in Haematology* 1985; **14:** 775.

Cardiovascular system

Physiology

The pre-thrombotic state. Davies, J.A. *Clinical Science* 1985; **69:** 641.

The opioid system and central cardiovascular control: analysis of controversies. Feuerstein, G. *Peptides* 1985; **6:** 51 (Suppl 2).

Cardiovascular effects of positive end-expiratory pressure (PEEP) after pneumonectomy in dogs. Lores, M.E., Keagy, B.A. *et al. Annals of Thoracic Surgery* 1985; **40:** 464.

Effect of vasoactive intestinal polypeptide on the canine cardiovascular system. Unverferth, D.V., O'Dorisio, T.M. *et al. Journal of Laboratory and Clinical Medicine* 1985; **106:** 542.

The role of lung innervation in the hemodynamic response to hypertonic sodium chloride solutions in hemorrhagic shock. Younes, R.N., Aun, F. *et al. Surgery* 1985; **98:** 900.

Treatment and medication

Efficacy and safety of esmolol vs propranolol in the treatment of supraventricular tachyarrhythmias: a multicenter double-blind clinical trial. Abrams, J., Allen, J. *et al. American Heart Journal* 1985; **110:** 913.

Towards better resuscitation. Baskett, P.J. *British Journal of Hospital Medicine* 1985; **34:** 345.

Hemodynamic and renal function in essential hypertension during treatment with enalapril. Bauer, J.H., Reams, G.P. *American Journal of Medicine* 1985; **79:** 10.

Antifibrillatory effects of lidocaine and bretylium immediately after postcardiopulmonary resuscitation. Chow, M.S.S., Kluger, J. *et al. American Heart Journal* 1985; **110:** 938.

Severe hypotension after first dose of enalapril in heart failure. Cleland, J.G.F., Dargie, H.J. *et al. British Medical Journal* 1985; **291:** 1309.

Interaction of the effects of hypoxia, substrate depletion, acidosis and hyperkalaemia on the class III antiarrhythmic properties of sotalol. Cobbe, S.M., Manley, B.S., Alexopoulos, D. *Cardiovascular Research* 1985; **19:** 668.

Norepinephrine infusions in congestive heart failure. Goldsmith, S.R., Francis, G.S., Cohn, J.N. *American Journal of Cardiology* 1985; **56:** 802.

Ventilatory effects of atenolol and bevantolol in asthma. Jan-Willem, J., Lammers, M.D. *et al. Clinical Pharmacology and Therapeutics* 1985; **38:** 428.

Suppression of positive inotropic and toxic effects of cardiac glycosides by amiloride. Kennedy, R.H., Akera, T., Brody, T.M. *European Journal of Pharmacology* 1985; **115:** 199.

200 years of digitalis: the emerging central role of the sodium ion in the control of cardiac force. Lee, C.O. *American Journal of Physiology* 1985; **249:** C367.

Inotropic drugs for the treatment of heart failure. Mancini, D.M., Keren, G. *et al. Journal of Clinical Pharmacology* 1985; **25:** 540.

Cellular mechanisms of digitalis action. Miura, D.S., Biedert, S. *Journal of Clinical Pharmacology* 1985; **25:** 490.

Treatment of hypertension with calcium antagonists. Murphy, M.B. *International Journal of Clinical Pharmacology Research* 1985; **5:** 287.

Mexiletine: double-blind comparison with procainamide in PVC suppression. Nademanee, K., Feld, G. *et al. American Heart Journal* 1985; **110:** 923.

Hemodynamic evaluation of blood transfusion in chronic severe anemia with special reference to speed of transfusion. Nand, N., Gupta, S.P., Gupta, M.S. *Japanese Heart Journal* 1985; **26:** 759.

Circulating catecholamine and potassium concentrations early in acute myocardial infarction: effect of intervention with timolol. Nordrehaaug, J.E., Johannessen, K.-A. *et al. American Heart Journal* 1985; **110:** 944.

Comparative effects of vasodilator drugs on flow distribution and venous return. Ogilvie, R.I. *Canadian Journal of Physiology and Pharmacology* 1985; **63:** 1345.

Progress in cardiac pacing. Shively, B., Goldschlager, N. *Archives of Internal Medicine* 1985; **145:** 2103.

Digitalis: neurally mediated arrhythmogenic and coronary vasoconstrictor properties. Somberg, J.C. *Journal of Clinical Pharmacology* 1985; **25:** 529.

Changes in blood pressure, fluid volumes and glomerular filtration rate during long-term treatment with prizidilol. Steen Andersen, G., Hartling, O.J. *et al. Danish Medical Journal* 1985; **32:** 280.

Pharmacokinetic differences between peripheral and central drug administration during cardiopulmonary resuscitation. Talit, U., Braun, S. *et al. Journal of the American College of Cardiology* 1985; **6:** 1073.

Respiration

Physiology

Breathlessness during different forms of ventilatory stimulation: a study of mechanisms in normal subjects and respiratory patients. Adams, L., Lane, R. *et al. Clinical Science* 1985; **69:** 663.

Bronchial circulation in asthma. Baier, H., Long, W.M., Wanner, A. *Respiration* 1985; **48:** 199.

Mediators and asthma. Barnes, P.J. *British Journal of Hospital Medicine* 1985; **34:** 339.

Activation of the human diaphragm during maximal static efforts. Gandevia, S.C., McKenzie, D.K. *Journal of Physiology* 1985; **367:** 45.

Respiratory sensation in chronic obstructive pulmonary disease. Gottfried, S.B., Redline, S., Altose, M.D. *American Review of Respiratory Disease* 1985; **132:** 954.

Immunologic lung disease. Harman, E.M. *Medical Clinics of North America* 1985; **69:** 705.

Respiratory muscle activity and thoracoabdominal motion during acute episodes of asthma during sleep. Issa, F.G., Sullivan, C.E. *American Review of Respiratory Disease* 1985; **132:** 999.

Influence of lung and chest wall compliances on transmission of airway pressure to the pleural space in critically ill patients. Jardin, F., Genevray, B. *et al. Chest* 1985; **88:** 653.

Oxygen toxicity and restructuring of pulmonary arteries. A morphometric study: the response to 4 weeks' exposure to hyperoxia and return to breathing air. Jones, R., Zapol, W.M., Reid, L. *American Journal of Pathology* 1985; **121:** 212.

The adult respiratory syndrome. Review. Norwood, S.H., Civetta, J.M. *Surgery Gynecology and Obstetrics* 1985; **161:** 497.

Factors influencing pulmonary volumes and CO_2 elimination during high-frequency jet ventilation. Rouby, J.J., Simonneau, G. *et al. Anesthesiology* 1985; **63:** 473.

Collapsibility of the nasopharyngeal airway in obstructive sleep apnea. Surratt, P.M., McTier, R.F., Wilhoit, S.C. *American Review of Respiratory Disease* 1985; **132:** 967.

Diaphragmatic strength during weaning from mechanical ventilation. Swartz, M.A., Marino, P.L. *Chest* 1985; **88:** 736.

High-frequency oscillatory ventilation and pulmonary extravascular water. Tamura, M., Kawano, T. *et al. Anesthesia and Analgesia* 1985; **64:** 1041.

Adenosine stimulates respiration in man. Watt, A.H., Routledge, P.A. *British Journal of Clinical Pharmacology* 1985; **20:** 503.

The effects of nasal anesthesia on breathing during sleep. White, D.P., Cadieux, R.J. *et al. American Review of Respiratory Disease* 1985; **132:** 972.

Treatment and medication

Clinical application of continuous flow apneic ventilation. Babinski, M.F., Sierra, O.G. *et al. Acta Anaesthesiologica Scandinavica* 1985; **29:** 750.

The intensive care of asthma. Branthwaite, M.A. *British Journal of Hospital Medicine* 1985; **34:** 331.

Ventilator settings and active expiration. Field, D., Milner, A.D., Hopkin, I.E. *Archives of Disease in Childhood* 1985; **60:** 1036.

Does intermittent mandatory ventilation correct respiratory alkalosis in patients receiving assisted mechanical ventilation. Hudson, L.D., Hurlow, R.S. *et al. American Review of Respiratory Disease* 1985; **132:** 1071.

The treatment of asthma. Part 2. Practical aspects of management. Paterson, J.W., Tarala, R.A. *Medical Journal of Australia* 1985; **143:** 453.

The treatment of asthma. Part 1, pharmacology of therapeutic agents. Paterson, J.W., Tarala, R.A. *Medical Journal of Australia* 1985; **143:** 390.

Central nervous system

Physiology

The grey matter of the dorsal horn of the adult human spinal cord. Abdel-Maguid, T.E., Bowsher, D. *Journal of Anatomy* 1985; **142:** 33.

Sleep-apnea in normal subjects following mandibular osteotomy with retrusion. Guilleminault, C., Riley, R., Powell, N. *Chest* 1985; **88:** 776.

The cerebrospinal fluid in myasthenia gravis. Thorlacius, S., Aarli, J.A. *Acta Neurologica Scandinavica* 1985; **72:** 532.

Clinical neurophysiology of conduction in central motor pathways. Young, R.R., Cracco, R.Q. *Annals of Neurology* 1985; **18:** 606.

Treatment and medication

Pharmacokinetics of high-dose pentobarbital in severe head trauma. Bayliff, C.D., Schwartz, M.L., Hardy, B.G. *Clinical Pharmacology and Therapeutics* 1985; **38:** 457.

Evidence for the pharmacological relevance of benzodiazepine receptors to anticonvulsant activity. Fisher, T.E., Johnson, D.D. *et al. Canadian Journal of Physiology and Pharmacology* 1985; **63:** 1477.

Contrasting actions of naloxone in experimental spinal cord trauma and cerebral ischemia: a review. Hamilton, A.J., Black, P.M. *Neurosurgery* 1985; **17:** 845.

Anesthesia and surgery in the seated position: analysis of 554 cases. Matjasko, J., Petrozza, P. *et al. Neurosurgery* 1985; **17:** 695.

Metabolic and nutritional sequelae in the non-steroid treated head injury patient. Young, B., Ott, L. *et al. Neurosurgey* 1985; **17:** 784.

Endocrine and metabolic

Physiology

Blood to interstitial fluid volume ratio in chronic hypokalaemic states. Boer, P., Koomans, H.A. *et al. European Journal of Clinical Investigation* 1985; **15:** 276.

The effects and interactions of angiotensin and vasopressin on the heart of unanaesthetized sheep. Caine, A.C., Lumbers, E.R., Reid, I.A. *Journal of Physiology* 1985; **367:** 1.

The calcium signal. Carafoli, E., Penniston, J.T. *Scientific American* 1985; **253:** 70.

Minireview. Somatostatin: a metabolic regulator. Dileepan, K.N., Wagle, S.R. *Life Sciences* 1985; **37:** 2335.

Mechanism of action of thyroid hormones. Dillman, W.H. *Medical Clinics of North America* 1985; **69:** 849.

Blood pressure effects of acute hypercalcemia in normal subjects and thyroparathyroidectomized patients. Gennari, C., Nami, R. *et al. Mineral and Electrolyte Metabolism* 1985; **11:** 369.

The effect of hypoglycaemia on visual function: a clinical and electrophysiological study. Harrad, R.A., Cockram, C.S. *et al. Clinical Science* 1985; **673:** 69.

Biosynthesis of the insulin receptor. Hedo, J.A., Gorden, P. *Hormone and Metabolic Research* 1985; **17:** 487.

Dynamic changes in serum phosphorous levels in diabetic ketoacidosis. Kebler, R., McDonald, D., CADNAPHAPHORNCHI, P. *American Journal of edicine* 1985; **79:** 571.

l measurement of plasma vasopressin in the wborn. MCINTOSH, N., SMITH, A. *Archives of iseases in Childhood* 1985; **60:** 1031.

cts of volume expansion on renal nerve activity, nal blood flow, and sodium and water excretion in onscious dog. MORITA, H., VATNER, S.F. *et al. merican Journal of Physiology* 1985; **249:** F680.

ntrasting effects of vasopressin on baroreflex nhibition of lumbar sympathetic nerve activity. SHARABI, F.M., GUO, G.B. *et al. American Journal of Physiology* 1985; **249:** H922.

egulation of vasopressin secretion in a patient with chronic hypernatraemia. SMITH, S., LEGROS, J.J. *Acta Endocrinologica* 1985; **110:** 346.

High molecular weight vasopressin—detection of a large amount in the plasma of a patient. SMITHZM, S., LEGROS, J.J. *et al. Clinical Endocrinology* 1985; **23:** 379.

Effect of potassium depletion on acidosis-induced changes in plasma potassium concentration. VAAMONDE, C.A., OSTER, J.R. *et al. Mineral and Electrolyte Metabolism* 1985; **11:** 381.

Vasopressin: site of behavioral action and role in human mental performance. VAN WIMERSMA GREIDANUS, T., VELDHUIS, H. *Peptides* 1985; **6:** 177 (Suppl 2).

Studies of the central cardiovascular effects of vasopressin. ZERBE, R.L. *Peptides* 1985; **6:** 65 (Suppl 2).

Treatment and medication

The effect of naloxone on ATCH and beta-endorphin in patients with Cushings disease. BARANOWSKA B., DOROBEK, W. *et al. Acta Endocrinologica* 1985; **110:** 170.

Dual actions of sulfonylureas and glyburide: receptor and post-receptor effects. GAVIN, J.R. *American Journal of Medicine* 1985; **79:** 34.

Effects of calcium antagonists on renal hemodynamics. LOUTZENHISER, R., EPSTEIN, M. *American Journal of Physiology* 1985; **249:** F619.

Diuretic-associated hypokalemia. MATERSON, B.J. *Archives of Internal Medicine* 1985; **145:** 1966.

Platelet function during continuous insulin infusion treatment in insulin-dependent diabetic patients. MAYFIELD, R.K. *et al. Diabetes* 1985; **34:** 1127.

New insights into the pharmacokinetics of spironolactone. OVERDICK, H.W.P.M., HERMENS, A.J.J. *et al. Clinical Pharmacology and Therapeutics* 1985; **38:** 469.

New class of inhibitors specific for human renin. PAPAIOANNOU, S., HANSEN, D. *et al. Clinical and Experimental Hypertension. Part A—Theory and Practice* 1985; **7:** 1243.

Pain

Treatment and medication

Postoperative analgesia following thoracotomy. BROWN, D.L. *Chest* 1985; **88:** 779.

Other

Physiology

Relation between antral motility and gastric emptying of solids and liquids in humans. CAMILLERI, M., MALAGELADA, J.-R. *et al. American Journal of Physiology* 1985; **249:** G580.

Pathophysiology of gastroesophageal reflux. SKINNER, D.B. *Annals of Surgery* 1985; **202:** 546.

Erratum

Anaesthesia, 1986, Volume 41, page 687

Halothane and trichloroethylene

Two agents in a single vaporizer

N. HOLLIS

We regret that in this article the diagrams for Figs 3 and 4 were accidentally transposed and, similarly the diagrams for Figs 5 and 6. Corrected reprints are available from the author.

Anaesthesia, Volume 41, page 688

Hazard notice

Ether explosion during anaesthesia

A recent incident which involved the use of diethyl ether resulted in an explosion which caused fatal injury to a patient. The most likely source of ignition was the cautery probe which was in use at the time within the zone of risk, that is within 25 cm of the breathing system. Flammable anaestheic agents should not be used in the presence of an ignition source such as cautery (hot wire) diathermy or laser. Electrical equipment used within the 25 cm Zone of Risk must comply with the requirements of BS5724 Part I and be marked Anaesthetic Proof Category G Equipment (APG) or Anaesthetic Proof Equipment (AP) depending upon the distance from the breathing system. Antistatic precautions must be taken to avoid electrostatic sparking in areas where inflammable anaesthetics are administered. The recommendations in HTM 1 and HTM 2 need to be strictly adhered to.

The need to use flammable anaesthetic agents should be reviewed by anaesthetists.

Stop press

International Congress Calendar

1986

20–25 September. Hong Kong. *7th Asian and Australasian Congress of Anaesthesiologists.*
Information: 7AACA Secretariat, c/o International Conference Consultants, 1st Floor, 5 Wyndham Street, Central, Hong Kong.

THIS PAGE CONCERNS YOU IF YOU ARE A MEDICALLY QUALIFIED ANAESTHETIST IN GREAT BRITAIN AND IRELAND, OVERSEAS OR IN TRAINING AND ARE NOT YET A MEMBER OF THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND OR IF YOU ARE A MEMBER OF ANOTHER PROFESSION WHO PRACTISES IN ANAESTHESIA AND YOU WISH TO APPLY FOR ASSOCIATE MEMBERSHIP

Ordinary Membership (*United Kingdom and Ireland only*)

Voting membership of the Association (the only effective body representing anaesthetists' interests in non-academic matters).

The right of attendance at the Annual General and Scientific Meetings and all other meetings of the Association of Anaesthetists.

Overseas and Associate Membership

The right of attendance at the Annual Scientific Meeting and other meetings of the Association.

Junior Membership (*United Kingdom and Ireland only*)

Voting membership of the Association.

Representation of the Council of the Association. The Chairman and Secretary of the Junior Group sit on Council as voting members.

Attendance at the Annual Scientific Meeting of the Association and at the special Annual Scientific Meeting of the Junior Anaesthetists' Group, at which Junior Members of the Association are given preference.

Membership Fees (inclusive of the journal *Anaesthesia*)

Ordinary Members: Entrance Fee **£5**, Subscription **£60** (Husband and wife **£48** each)

Overseas and Associate Members: No Entrance Fee, Subscription **£60**

Junior Members: No Entrance Fee, Subscription **£36** (**£48** after 3 years if still in training)

Retired Members: who receive *Anaesthesia* **£10** (there is no subscription for those who do not).

How to apply for membership

Fill in the application form on the other side of this page.

Have it countersigned by two members of the Association, one of whom must be an Ordinary Member.

Tear out the page and send it to the address indicated overleaf.

Do not send money with your application

THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND

APPLICATION FOR MEMBERSHIP

to

The Association of Anaesthetists of Great Britain and Ireland
9 Bedford Square,
London WC1B 3RA, England

(This application will be considered by Council at its next meeting. NO MONEY should be sent in the meantime. After acceptance of the application by Council, the Hon. Secretary will notify the applicant of Council's decision and the amount of subscription payable in the current financial year.)

........................19

To the Honorary Secretary,
Association of Anaesthetists of Great Britain and Ireland

I (full name).. offer my name as a candidate
BLOCK LETTERS

for (a) MEMBERSHIP (b) OVERSEAS MEMBERSHIP (c) ASSOCIATE MEMBERSHIP (d) JUNIOR MEMBERSHIP of the Association (*please delete categories not applicable*)*

I hold the following appointment(s) as an anaesthetist (*please state grade if in the National Health Service, and indicate the approximate proportion of time spent in the practice of anaesthesia*):

....

....

....

Qualifications (with dates)..

....

(Signed)...

Address...

....Hospital Tel. No:.......................................

....Home Tel. No:..

We, being Members† of the Association, nominate as a candidate for MEMBERSHIP/OVERSEAS/ASSOCIATE/JUNIOR MEMBERSHIP

....

1. (Signed)...
(NAME IN BLOCK LETTERS)

Address...
BLOCK LETTERS

2. (Signed)...
(NAME IN BLOCK LETTERS)

Address...
BLOCK LETTERS

* See the reverse of this page for details of membership categories.
† One sponsor must be an Ordinary Member of the Assocation.

Notice to contributors to *Anaesthesia*

Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Articles accepted become copyright of *Anaesthesia.*

Contributors are requested to submit two copies of manuscripts. They are also advised to retain a third copy as the Editors cannot accept responsibility for the loss of manuscripts in the post. The covering letter should be signed personally by all the authors and careful consideration should be given to the decision to include more than five authors. Articles should be forwarded to:

Dr J. N. Lunn, Editor of ***Anaesthesia****, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.*

PREPARATION OF MANUSCRIPTS

Articles for *Anaesthesia* should be prepared in accordance with *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5) except that the titles of journals in the reference section should be given in full (see below). A reprint of these requirements of which this notice is a summary, can be obtained from the *British Medical Journal* price 50 pence (U.K.).

Type manuscripts on white bond paper, 20.3 × 26.7 cm or 21.6 × 27.9 cm (8 × 10½ in. or 8½ × 11 in.) or ISO A4 (212 × 297 mm) with margins of at least 2.5 cm (1 in.). Use double, and preferably triple, spacing throughout, including the references. Please do not use a dot matrix printer, particularly one with poor quality descenders or ascenders. Unseparated, fan-folded manuscripts may be returned to the author.

The manuscript should consist of the following sections in this order each beginning on a new page: *title page, summary* and *key words, text, acknowledgments, references, individual tables,* and *legends for figures.*

Number pages consecutively, beginning with the title page. Type the page number in the upper right-hand corner of each page.

THE TITLE PAGE

The name of the author and the address to which proofs and other correspondence is to be addressed should appear in the top left-hand corner of the sheet.

The main title should be restricted to five words if this is possible. It should be typed in capitals across the centre of the title page.

A subsidiary title of not more than 12 words may be supplied if this is considered to be necessary. This should be typed in lower case immediately beneath the main title.

The names of the authors should be typed IN CAPITALS across the title page immediately beneath the titles without degrees or designations. Initials should precede the surname. One forename may be given in full according to the author's preference. If there is more than one author the word 'AND' should be placed before the name of the last author.

A line should be typed across the title page below the author(s) name(s) in capitals.

The author(s) name(s) degrees and designations should be typed in lower case below the line. Initials and/or forename should precede the name of each author and his degrees, without full stops between letters, and appointment (e.g. Consultant, Registrar, etc.) should follow it.

A full postal institutional address should follow the names, degrees and appointments. Correspondence will normally be addressed to the first author but, if it is desired to direct correspondence other than to the first author, or if different authors belong to different institutions or departments, a separate sentence should be added; this should start on a new line and begin 'Correspondence should be addressed to . . .' and a full postal address should follow.

SUMMARY AND KEY WORDS

Start a new sheet

The second page should carry a summary of not more than 150 words. The summary should state the purpose of the study or investigation, basic procedures, main findings and their statistical significance, and the principal conclusions.

Do not use abbreviations except for units of measurement (e.g. mg, cm, etc.).

Key (indexing) words. Below the abstract, provide and identify as such, three to 10 key words or short phrases that will assist indexers. Use terms from the Medical Subject Headings list from *Index Medicus.* The Editor may modify these at proof stage to conform with agreed practice of certain other anaesthetic journals in the English language.

COPYRIGHT OFFPRINTS

Authors submitting a manuscript do so on the understanding that if it is accepted for publication, exclusive copyright in the paper shall be assigned to the Association. In consideration for the assignment of copyright, the Publisher will supply 25 offprints of each paper. Further offprints may be ordered at extra cost; the copyright assignment form and the offprint order form will be sent with the proofs. The Association will not put any limitation on the personal freedom of the author to use material contained in the paper in other works.

(*continued overleaf*)

THE TEXT

Start a new sheet

The text of observational and experimental articles, case reports, etc. is usually divided into sections with the headings *Introduction, Methods, Results* and *Discussion.* Long articles will need subheadings within some sections to clarify their content.

Letters for the correspondence pages should be double spaced and prepared in accordance with the format in a recent copy of *Anaesthesia.*

Headings: three steps of heading may be used in typescripts:

(i) CAPITALS across the centre of the page.

(ii) Underlined words

These should be typed at the left hand side of the page above the paragraph which they precede.

(iii) Underlined words at the beginning of a paragraph. These may either be followed by a full stop or form part of the first sentence of the paragraph.

ACKNOWLEDGMENTS

Start a new sheet

Acknowledge those who have made substantive contributions to the study or the preparation of the manuscript. Authors are responsible for obtaining written permission for publication of reproduced figures and tables from authors and publishers and from everyone acknowledged by name because of copyright conventions and because readers may infer their endorsement of the data and conclusions.

REFERENCES

Start a new sheet

Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by arabic numerals. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. Use double or treble space typing.

Use the form of reference adopted by the U.S. National Library of Medicine and used in *Index Medicus.* Use the style of the examples cited at the end of this section.

The titles of journals should be given in full.

Avoid using abstracts as references except those published in a recognised journal. 'Unpublished observations' and 'personal communications' may not be used as references, although references to written, not verbal, communications may be inserted (in parentheses) in the text. Include among the references manuscripts accepted but not yet published; designate the journal followed by (*in press*) in parentheses. Information from manuscript submitted but not yet accepted should be cited in the text as (unpublished observations) in parentheses.

The references must be verified by the author(s) against the original documents.

Examples of correct form of references

Note: first and last pages in all references.

JOURNAL

Standard journal article—(List all authors)

Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294:** 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

Osler AG. *Complement: mechanisms and functions.* New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. AMA drug evaluations. 3rd ed. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

Rhodes AJ, Van Rooven CE, *comps. Textbook of virology; for students and practitioners of medicine and other health sciences.* 5th ed. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

Weinstein L, Swartz MN Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease.* Philadelphia: WB Saunders, 1974; 457–72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, Md: National Center for Health Statistics, 1972. (*Vital and health statistics. Series* **10:** Data drom the National Health Survey, No. 69) [DHEW publication No. (HSM) 72-1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

ROUECHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

TABLES

Do not include tables in the text. Start a new sheet for each table and space the material adequately. The author(s) name(s) should appear in the top right-hand corner.

Indicate the approximate position of each table in relation to the subject matter of the text in the right-hand margin of the appropriate page on the manuscript. Do not submit tables as photographs. Number tables consecutively with arabic numerals. Supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes. Explain in footnotes all non-standard abbreviations that are used in each table. For footnotes, use the following symbols in this sequence: *, †, ‡, §, ||, ¶, **, ††, etc. Identify statistical measures of variations such as SD and SEM. *Legends for tables* should appear on the face of the table.

Cite each table in the text in consecutive order and mark the approximate position of the table in the right-hand margin of the text.

FIGURES

Each figure should be separate. Do not include figures in the text but collect together in an envelope or folder.

Indicate the approximate position of each figure in relation to the subject matter of the text in the right-hand margin of the appropriate page of the manuscript. Drawings, charts and diagrams should be submitted in black indian ink on a smooth white card and should be about twice the size of that desired in the published version with no lettering. Full plate, glossy black and white photographs will be accepted if they are sufficiently clear. All letters and numerals required on the face of figures must be clearly typed or written on tracing paper firmly attached with self-adhesive tape to the back of the figure and folded over from the front as a cover. They will then be printed in the style of *Anaesthesia* in the exact location indicated. Identify each figure by its sequential number in pencil on the reverse of the illustration and include the title of the paper and the authors' names. Mark the top of the illustration on the reverse by an arrow and the word 'Top'.

All sources of identification of patients must be removed.

LEGENDS FOR FIGURES

Start a new sheet

Type legends for illustrations double spaced with arabic numerals corresponding to the illustrations. When symbols, arrows, numbers or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

CONVENTIONS AND ABBREVIATIONS

Statistics and measurements should be given in figures except that numerals one to nine should be in words if not followed by a measurement symbol (e.g. 'two patients' but '2.0 mg'). The *Système International* (SI) will usually be used except that vascular pressures will be recorded in mmHg and cmH_2O. Imperial measurements will not be used except in an historic context. The 24 hour clock will be used.

Contributors are advised to study the SI *Conversion Tables* provided in the January 1978 issue of *Anaesthesia, Units, Symbols and Abbreviations* (*A Guide for Biological and Medical Editors and Authors*) published by the Royal Society of Medicine, London W1M 8AE, and *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1**: 532–5).

LETTERS FOR PUBLICATION

Should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University of Wales Hospital, Heath Park, Cardiff CF4 4XW, UK.

Letters should be typewritten on one side of the paper only and double spaced with wide margins. Copy should be prepared in the usual style and format of the Correspondence section. Authors must follow the advice about references and other matters above. The degrees and diplomas of each author must be given in a covering letter which must be signed personally by all the authors.

Correspondence presented in any other style or format may be the subject to considerable delay and may be returned to the author for revision.

The editors regret that failure to comply with the above requirements may result in a delay in publication of accepted papers.

REVIEW JOURNALS

This journal is covered by *Current Contents, ASCA* and the *Science Citation Index*.

Contents: Anaesthesia, vol. 41, no. 6, June 1986

EDITORIAL

Halothane hepatitis in children
B. Walton 575

ORIGINAL ARTICLES

Increased hepatic microsomal activity after halothane anaesthesia in children
O. St Haxholdt, S. Loft, A. Clemmensen and E.H. Hjortsø 579
The effects of continuous intravenous naloxone on epidural morphine analgesia
G.S. Thind, J.C.D. Wells and R.G. Wilkes 582
The influence of nitrous oxide on oxyhaemoglobin dissociation and measurement of oxygen tension
M.V. Shah, L.K. Anderson and N.A. Bergman 586
Propofol and alfentanil infusion. A comparison with methohexitone and alfentanil for major surgery
B. Kay 589

CASE REPORTS

Peri-operative management of carcinoid syndrome using ketanserin
K. Houghton and J.A. Carter 596
Anaphylaxis to precurarising doses of gallamine triethiodide
J.F. Harrison and A.G. Bird 600
Pulmonary occlusion (wedge) angiography in adult respiratory distress syndrome. A survey of angiographic appearances and outcomes
P.G. Lawler 605
Halothane hepatitis in an 11-month-old child
R.H. Whitburn and E. Sumner 611
Acute rhabdomyolysis following surgery for burns. Possible role of tourniquet ischaemia
P.M. Pfeifer 614
Intensive care aspects of severe *Legionella* pneumonia
K.J. Power and D.J. Bowen 620
Acute respiratory failure following lithium intoxication. A report of two cases
P.G. Lawler and J.R. Cove-Smith 623

APPARATUS

A new double lumen tube adaptor. Use in adjustment of bronchial cuff volume and oxygenation
A.N. Sibai and A. Baraka 628
No moving parts. A modification of a Bain system and a Penlon Nuffield 200 ventilator
M.N. Calhaem 631

FORUM

Intravenous fluids in minor surgery. Their effect on recovery from anaesthesia
P.W. Keane and P.F. Murray 635
Hypotensive anaesthesia for microsurgery of the middle ear. A comparison between isoflurane and halothane
M.L. Fairbairn, R.J. Eltringham, P.N. Young and J.M. Robinson 637
Intravenous anaesthesia with propofol and alfentanil. The influence of age and weight
P. Hilton, V.J. Dev and E. Major 640
Treatment of near drowning—a review of 130 cases
A.D. Simcock 643

CORRESPONDENCE 649

ANAESTHETIC LITERATURE 682

HAZARD NOTICE 688

STOP PRESS 688

Printed in Great Britain by Fletcher & Son Ltd, Norwich